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(54) BICYCLIC AMINO DERIVATIVES AND PGD 2 ANTAGONIST CONTAINING THE SAME

BIZYKLISCHE AMINODERIVATE UND ENTHALTENDE PGD2-ANTAGONISTEN

DERIVES AMINO BICYCLIQUES ET ANTAGONISTE DE PGD 2 CONTENANT CES DERIVES

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EP 0 837 052 B1

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Description

FIELD OF THE INVENTION

[0001] The present invention relates to bicyclic amino derivatives and prostaglandin D_2 (hereinafter, referred to as PDG_2) antagonist containing them.

BACKGROUND OF THE INVENTION

[0002] Some bicyclic amino derivatives are known to be useful as thromboxane A_2 (TXA_2) antagonists (Japanese Patent Publication No. JP63-139161). However, Japanese Patent Publication No. JP63-139161 only describes the compounds as useful as TXA_2 antagonists, and does not suggest usefulness thereof as PDG_2 antagonists.

[0003] Namely, TXA_2 is known to have activities such as action against platelet agglutination, thrombogenesis, etc. The TXA_2 antagonist has therefore been considered to be useful as an anti-thrombotic agent, and also in the treatment of myocardial infarction or asthma by antagonizing against TXA_2.

[0004] EP-A-608847 discloses carbocyclic sulfonamides as agonists or antagonists of PGEZ.

[0005] EP-A-312906 discloses sulfonamide derivates, which can be used as TXA_2 antagonists.

[0006] EP-A-0226346 discloses bicyclic sulfonamide derivatives, which can be used as antithrombotic, anti-vasoconstricting and anti-bronchoconstricting drugs.

[0007] EP-A-0150709 discloses 7-oxabicycloheptane prostaglandin analogs as cardiovascular agents, which are useful in the treatment of thrombolytic disease.

[0008] EP-A-0290285 discloses bicyclic sulfonamide derivatives and their use in the treatment of diseases such as angina pectoris, myocardial infarction and cerebral infarction.

[0009] A TXA_2 receptor antagonist, "S-1452", is disclosed in Int. Arc. Allergy Immunol. (1992) 98, 239-246, Arimura et al., "Antiasthmatic Activity of a Novel Thromboxane A2 Antagonist, S-1452, in Guinea Pigs" (XP 00 291 6327) .

[0010] On the other hand, the PGD_2 antagonist of the present invention is useful in the improvement of conditions due to excessive production of PGD_2. Specifically, it is useful as a drug for treating diseases in which mast cell dysfunction is involved, for example, systemic mastocytosis and disorder of systemic mast cell activation, and also tracheal contraction, asthma, allergic rhinitis, allergic conjunctivitis, urticaria, injury due to ischemic reperfusion, and inflammation.

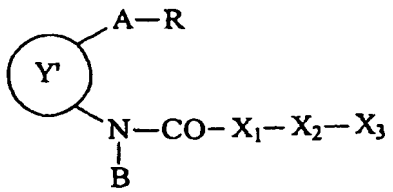
[0011] As is apparent from the above, the TXA_2 antagonist and the PGD_2 antagonist are completely different from each other in terms of the active site, mechanism of action, and application, and have quite different characteristics. Accordingly, it has never been expected that any compound could possess these activities simultaneously.

[0012] PGD_2 is produced through PGG, and PGH_2 from arachidonic acid by the action of cyclooxygenase activated by immunological or unimmunological stimulation and is the major prostanoid that is produced and released from mast cells. PGD_2 has various potent physiological and pathological activities. For example, PGD_2 can cause strong tracheal contraction, which leads to bronchial asthma, and, in a systemic allergic state, it can dilate the peripheral vessels, which leads to an anaphylactic shock. Especially, much attention has been paid to the idea that PGD_2 is one of the causal substances responsible for the onset of nasal occlusion in the allergic rhinitis. Therefore, it has been proposed to develop an inhibitor against the biosynthesis of PGD_2 or an antagonist of PGD_2 receptor as a drug for the reduction of nasal occlusion. However, the inhibitor of PGD_2 biosynthesis possibly affects greatly the synthesis of prostaglandins in other organisms, and therefore, it is desirable to develop an antagonist (blocker) specific to PGD_2 receptor.

DISCLOSURE OF THE INVENTION

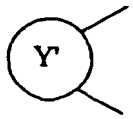
[0013] The present inventors have studied intensively to develop PGD_2 receptor antagonists (blockers) specific to PGD_2 receptor, and found that compounds of the formula (Ib) below or its salt possess a potent activity as PGD_2 receptor antagonists and are chemically and biochemically stable.

[0014] Accordingly, the present invention provides a PGD_2 antagonist which comprises a compound of the formula (Ib):

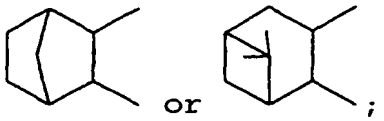


(Ib)

wherein



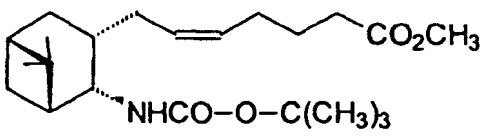
is



wherein A is alkylene which optionally is intervened by hetero atom or phenylene, contains oxo group, and/or has an unsaturated bond;

B is hydrogen, alkyl, aralkyl or acyl;
R is $COOR_1$, CH_2OR_2 or $CON(R_3)R_4$;
R_1 is hydrogen or alkyl;
R_2 is hydrogen or alkyl;
R_3 and R_4 each are independently hydrogen, alkyl, hydroxy or alkylsulfonyl;
X_1 is a single bond, phenylene, naphthylene, thiophenediyl, indolediyl, or oxazolediyl;
X_2 is a single bond, -N=N-, -N=CH-, -CH=N-, -CH=N-N-, -CH=N-O-, -C=NNHCSNH-, -C=NNHCONH-, -CH=CH-, -CH(OH)-, -C(C1)=C(Cl)-, $-(CH_2)_n-$, ethynylene, $-N(R_5)-$, $-N(R_{51})CO-$, $-N(R_{52})SO_2-$, $-N(R_{53})CON(R_{54})-$, $-CON(R_{55})-$ $-SO_2N(R_{56})-$, -O-, -S-, -SO-, $-SO_2-$, -CO-, oxadiazolediyl, thiadiazolediyl or tetrazolediyl;
X_3 is alkyl, alkenyl, alkynyl, aryl, aralkyl, heterocyclic group, cycloalkyl, cycloalkenyl, thiazolinylidenemethyl, thiazolidinylidenemethyl, $-CH=NR_6$ or $-N=C(R_7)R_8$;
R_5, R_{51}, R_{52}, R_{53}, R_{54}, R_{55} and R_{56}, each are hydrogen or alkyl;
R_6 is hydrogen, alkyl, hydroxy, alkoxy, carbamoyloxy, thiocarbamoyloxy, ureido or thioureido;
R_7 and R_8 each are independently alkyl, alkoxy or aryl;
and n is 1 or 2;

wherein a cyclic substituent may have one to three substituents selected from the group consisting of nitro, alkoxy, sulfamoyl, substituted- or
unsubstituted-amino, acyl, acyloxy, hydroxy, halogen, alkyl, alkynyl, carboxy, alkoxycarbonyl, aralkoxycarbonyl, aryloxycarbonyl, mesyloxy, cyano, alkenyloxy, hydroxyalkyl, trifluoromethyl, alkylthio, $-N=PPh_3$, oxo, thioxo, hydroxyimino, alkoxyimino, phenyl and alkylenedioxy, or its salt or hydrate thereof; with the proviso that compounds (a) wherein X_1 and X_2 are a single bond, and X_3 is phenyl; (b) wherein X_1 is a single bond, X_2 is -O-, and X_3 is benzyl;

(c) 

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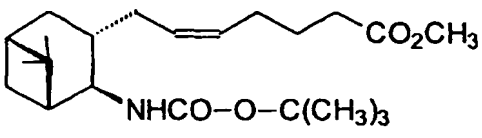
(d) 

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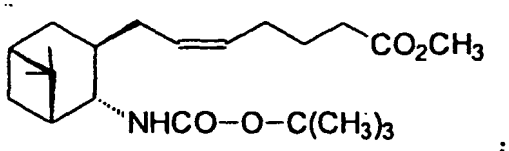
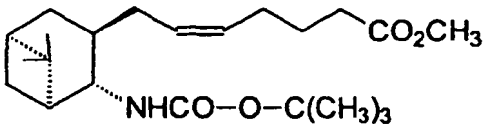


(e) ;

and



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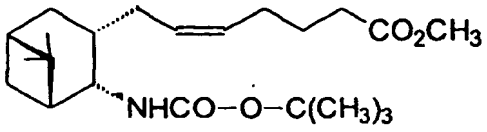
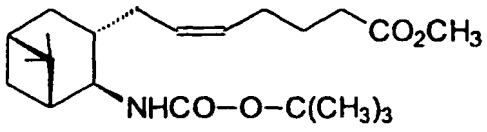
are excluded.

[0015] The compounds of the formulae:



(c) ;



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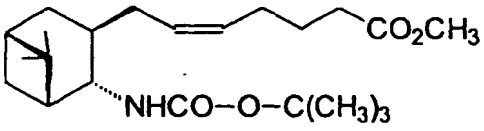
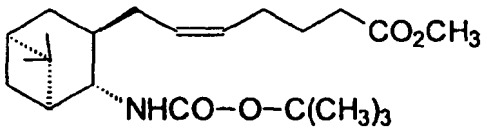


(e) ;

and



(f)

are excluded from the scope of claim 1 of this application/patent by way of disclaimers, which were introduced into the specification after filing the application. One or more of these compounds appears in each of EP-A-226346, EP-A-290285 and Chem. Pharm. Bull. 37(6), 1524-1533, K. Seno, S. Hagishita, "Thromboxane A2 Receptor Antagonists III. Synthesis and Pharmacological Activity of 6,6-Dimethylbicyclo[3.1.1]heptane Derivatives with a Substituted Sulfonylamino Group C-2," XP2058537. These compounds have been disclaimed as accidental anticipations, in accordance with the Decisions G1/03 and G2/03.

[0016] Examples of more preferred compounds include those of the formula (Ib) wherein R is $COOR_1$ (R_1 is as defined above) or a salt or hydrate thereof.

[0017] Similarly, examples of the compounds of the present invention include those of the formula (Ib) wherein X_1 is a phenylene or thiophenediyl, X_2 is a single bond, -N-N-, - CH=CH-, ethynylene, -O-, -S-, -CO-, -CON (R_{55}) - (R_{55} is as defined above), -N(R_{51})CO- (R_{51} is as defined above) and X_3 is phenyl, or a salt or hydrate thereof.

[0018] Examples of more preferred embodiments include those wherein B is hydrogen, both X_1 and X_2 are a single bond, X_3 is thienyl, thiazolyl, thiadiazolyl, isothiazolyl, pyrrolyl, pyridyl, benzofuryl, benzimidazolyl, benzothienyl, dibenzofuryl, dibenzothienyl, quinolyl or indolyl or a salt or hydrate thereof. Similarly, examples include those wherein X_1 is phenylene, thiophenediyl, indolediyl or oxazolediyl, X_2 is a single bond, -N=N-, ethynylene, -S-or -O-, and X_3 is aryl or heterocyclic group, or a salt or hydrate thereof.

[0019] The compounds of the general formula (Ib) are novel compounds synthesized by the present inventors.

[0020] The terms used throughout the present specification are as defined below.

[0021] The term "alkylene" means C_1- C_9 straight or branched chain alkylene, for example, methylene, methylmethylene, dimethylmethylene, methylethylmethylene, ethylene, trimethylene, tetramethylene, pentamethylene, hexamethylene, heptamethylene, octamethyene, nonamethylene , or the like. The alkylene above can be intervened by a hetero atom(s) (oxygen, sulfur, nitrogen atom, or the like) or phenylene (e.g., 1,4-phenylene, 1,3-phenylene, 1,2-phenylene, or the like), contain an oxo group, and/or have one or more double- or triple-bonds at any positions on the chain. Examples include -$(CH_3)_2$-O-CH_2-, -$(CH_2)_2$-O-$(CH_2)_2$-, -$(CH_2)_2$-O-$(CH_2)_3$-, -$(CH_2)_2$-O-$(CH_2)_4$-, -$(CH_2)_2$-O-$(CH_2)_5$-, -$(CH_2)_2$-O-$(CH_2)_6$-, -$(CH_2)_2$-S-$(CH_2)_2$-, -$(CH_2)_3$-S-$(CH_2)_2$-, -CH_2-S-CH_2-, -CH_2-S-$(CH_2)_4$-, -CH_2-N(CH_3)-CH_2-, -CH_2-NH-$(CH_2)_2$-, -$(CH_2)_2$-N(CH_2CH_3)-$(CH_2)_3$-, -$(CH_2)_2$-1,4-phenylene-CH_2-, -$(CH_2)_2$-O-1,3-phenylene-CH_2-, -$(CH_2)_2$-O-1,2-phenylene-CH_2-, -$(CH_2)_2$-O-1,4-phenylene-CH_2-, -CH=CH-S-CH_2-1,4-phenylene-CH_2-, -CH=CH-S-1,3-phenylene-$(CH_2)_2$-, 2-oxopropylene, 3-oxopentylene, 5-oxohexylene, vinylene, 1-propenylene, 2-propenylene, 1-butenylene, 2-butenylene, 3-butenylene, 1, 2-butadienylene, 1,3-butadienylene, 1-pentenylene, 2-pentenylene, 3-pentenylene, 4-pentenylene, 1,2-pentadienylene, 1, 3-pentadienylene, 1,4-pentadienylene, 2,3-pentadienylene, 2, 4-pentadienylene, 1-hexyenylene, 2-hexenylene, 3-hexenylene, 4-hexenylene, 5-hexenylene, 1,2-hexadienylene, 1,3-hexadienylene 1,4-hexadienylene, 1,5-hexadienylene, 2,3-hexadienylene, 2,4-hexadienylene 2,5-hexadienylene, 3,4-hexadienylene, 3,5-hexadienylene, 4,5-hexadienylen, 1,1-dimethyl-4-hexenylen, 1-heptenylene, 2-heptenylene, 3-heptenylene, 4-heptenylene, 5-heptenylene, 2,2-dimethyl-5-heptenylene, 6-heptenylene, 1,2-heptadienylne, 1,3-heptadienylene, 1,4-heptadienylene, 1,5-heptadienylene, 1,6-heptadienylene, 2,3-heptadienylene, 2,4-heptadienylene, 2,5-heptadienylene, 2,6-heptadienylene, 3,4-heptadienylene, 3,5-heptadienylene, 3, 6-heptadienylene, 4,5-heptadienylene, 4,6-heptadienylene or 5,6-heptadienylene, 1-propynylene, 3-butynylene, 2-pentynylene, 5-hexynylene, 6-heptynylene, -(CH_2)-CH=CH-O-$(CH_2)_2$-, -CH_2-S-$(CH_2)_3$-, -CH_2-cis-CH=CH-1,2-phenylene-CH,-, -CH=CH-1,4-phenylene-$(CH_2)_2$-, -4-oxo-4,5-hexenylene-, and the like.

[0022] The term "alkyl" means C_1 - C_{20} straight or branched chain alkyl, for example, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, i-pentyl, neopentyl, t-pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl, dodecyl, tridecyl, tetradecyl, pentadecyl, hexadecyl, heptadecyl, octadecyl, nonadecyl, icosyl, and the like.

[0023] The term "aryl" means C_6 - C_{14} monocyclic or condensed ring, for example, phenyl, naphthyl (e.g., 1-naphthyl, 2-naphtyl), anthryl (e.g., 1-anthryl, 2-anthryl, 9-anthryl), phenanthryl (e.g., 2-phenanthryl, 3-phenanthryl, 9-phenanthryl), fluorenyl (e.g., 2-fluorenyl), and the like. Phenyl is especially preferred.

[0024] The term "aralkyl" means a group formed by substituting an alkyl as defined above with an aryl above at any substitutable positions on the alkyl. Examples include benzyl, phenethyl, phenylpropyl (e.g., 3-phenylpropyl), naphtylmethyl (e.g., α-naphtylmethyl), anthrylmethyl (e.g., 9-anthrylmethy), phenanthrylmethyl (e.g., 3-phenanthrylmethyl), and the like.

[0025] The term "acyl" means C_1 - C_9 acyl derived from aliphatic carboxylic acid, for example, formyl, acetyl, propionyl, butyryl, valeryl, and the like.

[0026] The term "alkylsulfonyl" means a_group formed by substituting a sulfonyl with an alkyl above, for example, methylsulfonyl, ethylsulfonyl, propylsulfonyl, and the like.

[0027] The term "alkenyl" is C_2 - C_{20} straight or branched chain alkenyl, which corresponds to an alkyl above containing one or more double bonds. Examples include vinyl, 1-propenyl, 2-propenyl, 1-butenyl, 2-butenyl, 3-butenyl, 1,2-butadienyl, 1-pentenyl, 1,2-pentadienyl, 2-hexyenyl, 1,2-hexadienyl, 3-heptenyl, 1,5-heptadienyl, and the like. The term "alkynyl" is C_2 - C_{20} straight or branched chain, alkynyl, which corresponds to an alkyl above containing one or more triple bonds. Examples include ethynyl, 1-propynyl, 2-propynyl, 1-butynyl, 2-butyhyl, 3-butynyl, and the like.

[0028] The term "heterocyclic group" means 5 - 7 membered cyclic group containing one or more hetero atoms selected independently from the group consisting of oxygen, sulfur and/or nitrogen atom on the ring, and is optionally condensed with a carbon ring or other heterocyclic group at any substitutable positions. Examples include pyrrolyl (e.g., 1-pyrrolyl, 3-pyrrolyl), indolyl (e.g., 2-indolyl, 3-indolyl, 6-indolyl), carbazolyl (e.g., 2-carbazolyl, 3-carbazolyl), imidazolyl (e.g., 1-imidazolyl, 4-imidazolyl), pyrazolyl (e.g., 1-pyrazolyl, 3-pyrazolyl), benzimidazolyl (e.g., 2-benzimidazolyl, 5-benzimidazolyl), indazolyl (e.g., 3-indazolyl), indolizinyl (e.g., 6-indolyzinyl), pyridyl (e.g., 2-pyridyl, 3-pyridyl, 4-pyridyl), quinolyl

(e.g., 8-quinolyl), isoquinolyl (e.g., 3-isoquinolyl), acridyl (e.g., 1-acridyl), phenanthrydinyl (e.g., 2-phenanthrydinyl, 3-phenanthrydinyl), pyridazinyl (e.g., 3-gydidazinyl), pyrimidinyl (e.g., 4-pyrimidinyl), pyrazinyl (e.g., 2-pyrazinyl), cinnolinyl (e.g., 3-cinnolinyl), phthaladinyl (e.g., 5-phthaladinyl), quinazolinyl (e.g., 2-quinazolinyl), isoxazolyl (e.g., 3-isoxazolyl, 4-isoxazolyl), benzisoxazolyl (e.g., 1,2-benzisoxazol-4-yl, 2,1-benzisoxazol-3-yl), oxazolyl (e.g., 2-oxazolyl, 4-oxazolyl, 5-oxazolyl), benzoxazolyl (e.g., 2-benzoxazolyl), benzoxadiazolyl (e.g., 4-benzoxadiazolyl), isothiazolyl (e.g., 3-isothiazolyl, 4-isothiazolyl) benzisothiazolyl (e.g., 1,2-benzisothiazol-3-yl, 2,1-benzisothizol-5-yl), thiazolyl (e.g., 2-thiazolyl), benzothiazolyl (e.g., 2-benzothiazolyl), thiadiazolyl (e.g., 1,2,3-thiadiazol-4-yl), oxadiazolyl (e.g., 1,3,4-oxadiazol-2-yl), dihydroxadiazolyl (e.g., 4,5-dihydro-1,2,4-oxadiazol-3-yl), furyl (e.g., 2-furyl, 3-furyl), benzofuryl (e.g., 3-benzofuryl), isobenzofuryl (e.g., 1-isobenzofuryl), thienyl (e.g., 2-thienyl, 3-thienyl), benzothienyl (1-ber.zothiophen-2-yl, 2-benzothiophen-1-yl), tetrazolyl (e.g., 5-tetrazolyl), benzodioxolyl (e.g., 1,3-benzodioxol-5-yl), dibenzofuryl (e.g., 2-dibenzofuryl, 3-dibenzofuryl), dibenzoxepinyl (e.g., dibenz[b,f]oxepin-2-yl), dihydrodibenzoxepinyl (e.g., dihydrodibenz[b,f]oxepin-2-yl, chromenyl (e.g., 2H-chromen-3-yl, 4H-chromen-2-yl), dibenzothiepinyl (e.g., dibenzo[b,f]thiepin-3-yl, dihydrodibenzo [b,f]thiepin-3-yl), morpholinyl (e.g., 1,4-morpholin-4-yl), phenothiadinyl (2-phenothiadinyl), cyclopentathienyl (e.g., cyclopenta[b]thiophen-3-yl), cyclohexathienyl (e.g., cyclohexa[b]thiophen-3-yl), cycloheptathienyl (e.g., cyclohepta[b]thiophen-3-yl), dibenzothienyl (e.g., 2-dibenzothienyl), dibenzopyranyl (e.g., 2-dibenzopyranyl), dibenzo-p-dioxyl (e.g., 2-dibenzo-p-dioxyl), and the like.

[0029] The term "cycloalkyl" means C_3 - C_8 cyclic alkyl, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and the like.

[0030] The term "cycloalkenyl" means C_3- C_8 cyclic alkenyl, for example, cyclopropenyl (e.g., 1-cyclopropenyl), cyclobutenyl (e.g., 2-cyclobuten-1-yl), cyclopentenyl (1-cyclopenten-1-yl), cyclohexenyl (1-cyclohexen-1-yl), and the like.

[0031] The term "alkoxy" means C_1- C_6 alkoxy, for example, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, and the like.

[0032] Examples of the substituted amino in the definition of "substituted- or un-substituted-amino" include mono- or disubstituted amino such as methylamino, ethylamino, dimethylamino, cyclohexylamino, phenylamino, diphenylamino, or cyclic amino such as piperidino, piperadino or morpholino.

[0033] The term "acyloxy" means an acyloxy derived from the "acyl" above, for example, acetyloxy, propionyloxy, butyryloxy, valeryloxy, and the like.

[0034] The term "halogen" means fluorine, chlorine, bromine and iodine.

[0035] The term "alkoxycarbonyl" means an alkoxycarbonyl group derived from the "alkoxy" above, for example, methoxycarbonyl, ethoxycarbonyl, phenyloxycarbonyl, and the like.

[0036] The term "aralkyloxycarbonyl" means an aralkyloxycarbonyl group derived from the "aralkyl" above, for example, benzyloxycarbonyl, phenethyloxycarbonyl, and the like.

[0037] The term "aryloxycarbonyl" means an aryloxycarbonyl group derived from the "aryl" above, for example, phenyloxycarbonyl, naphtyloxycarbonyl, and the like.

[0038] The term "alkenyloxy" means an alkenyloxy group derived from the "alkenyl" above, for example, vinyloxy, 1-propenyloxy, 2-butenyloxy, and the like.

[0039] The term "hydroxyalkyl" means a hydroxyalkyl group derived from the "alkyl" above, for example, hydroxymethyl, hydroxyethyl, hydroxypropyl, and the like.

[0040] The term "alkylthio" means an alkylthio group derived from the "alkyl" above, for example, methylthio, ethylthio, propylthio, and the like.

[0041] The term "alkylenedioxy" means C_1 - C_3 alkylenedioxy, for example, methylenedioxy, ethylenedioxy, propylenedioxy, and the like.

[0042] In the case of "phenylene, "naphthylene", "thiophenediyl", "indolediyl", "oxazolediyl", "oxadiazolediyl" and tetrazolediyl", the said group can bind to the neighboring groups at any two substitutable sites.

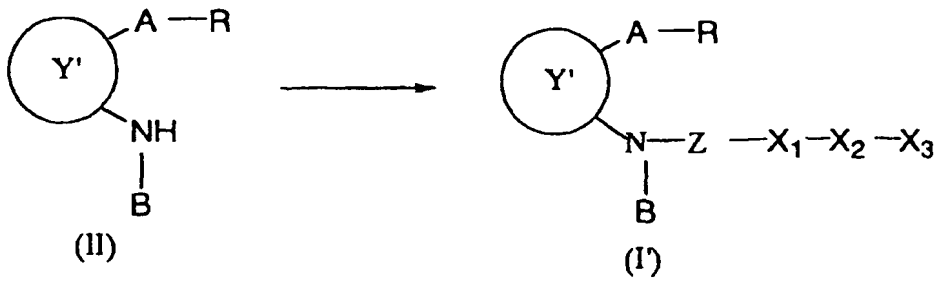
[0043] In the definitions above, when a substituent(s) is cyclic, it may be substituted by one to three substituents selected from nitro, alkoxy, sulfamoyl, substituted- or un-substituted-amino, acyl, acyloxy, hydroxy, halogen, alkyl, alkynyl, carboxy, alkoxycarbonyl, aralkoxycarbonyl, aryloxycarbonyl, mesyloxy, cyano, alkenyloxy, hydroxyalkyl, trifluoromethyl, alkylthio,-N=PPh_3, oxo, thioxo, hydroxyimino, alkoxyimino, phenyl and alkylenedioxy. The substituent(s) may bind to any substitutable positions on the ring.

[0044] Examples of salts of the compound (Ib) include those formed with an alkali metal (e.g., lithium, sodium or potassium), an alkaline earth metal (e.g., calcium), an organic base (e.g., tromethamine, trimethylamine, triethylamine, 2-aminobutane, t-butylamine, diisopropylethylamine, n-butylmethylamine, cyclohexylamine, dicyclohexylamine, N-isopropylcyclohexylamine, furfurylamine, benzylamine, methylbenzylamine, dibenzylamine, N,N-dimethylbenzylamine, 2-chlorobenzylamine, 4-methoxybenzylamine, 1-naphthylenemethylamine, diphenylbenzylamine, triphenylamine, 1-naphthylamine, 1-aminoanthoracene, 2-aminoanthoracene, dehydroabiethylamine, N-methylmorpholine or pyridine), an amino acid (e.g., lysine, or arginine), and the like.

[0045] The term "hydrate" means a hydrate of the compound of the formula (Ib) or its salt. Examples include mono- and dihydrates.

[0046] The present compounds are shown by the formula (Ib) and are inclusive of the form of any types of stereoisomers (e.g., diastereomer, epimer, enantiomer) and racemic compounds.

[0047] Compounds of the general formula (Ib) can be prepared by reacting an amino compound of the general formula (II) with a reactive derivative of sulfonic acid or carboxylic acid corresponding to the partial structure: $Z\text{-}X_1\text{-}X_2\text{-}X_3$ as shown below.



Wherein A, B, R, X_1, X_2, X_3, Y are as defined above and Z is -CO- A carboxylic acid corresponding to the said partial structure is a compound of the general formula $X_3\text{-}X_2\text{-}X_1\text{-}COOH$. Reactive derivative of these carboxylic acids means a corresponding halide (e.g., chloride, bromide, iodide), acid anhydride (e.g., mixed acid anhydride with formic acid or acetic acid), active ester (e.g., succinimide ester), and examples thereof generally include acylating agents used for the acylation of amino group. The carboxylic acid $X_3\text{-}X_2\text{-}X_1\text{-}COOH$ can be used in the reaction as it is without converting into a reactive derivative, in the presence of a condensing agent (e.g., dicyclohexylcarbodiimide (DCC), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, N,N'-carbonyldiimidazole) which are used in the condensing reaction between amine and carboxylic acid.

[0048] The reaction can be conducted under the conditions generally used for the acylation of amino groups. For example, in the case of condensation using an acid halide, the reaction is carried out using a solvent such as an ether solvent (e.g., diethylether, tetrahydrofuran, dioxane), benzene solvent (e.g., benzene, toluene, xylene), halogenated hydrocarbon solvent (e.g., dichloromethane, dichloroethane, chloroform), ethyl acetate, dimethylformamide, dimethyl sulfoxide, acetonitrile, or the like, if necessary, in the presence of a base (e.g., organic base such as triethylamine, pyridine, N,N-dimethylaminopyridine, N-methylmorpholine; inorganic base such as sodium hydroxide, potassium hydroxide, potassium carbonate, or the like) under cooling, at room temperature or under heating, preferably at temperature ranging from -20°C to a temperature under cooling, or from room temperature to a refluxing temperature of the reaction system, for several min to several hr, preferably for 0.5 hr to 24 hr, more preferably, for 1 hr to 12 hr.

[0049] The reaction conditions for the reaction between other reactive derivative or a free acid and an amine (II) can be determined in a conventional manner depending on the characteristics of the respective reactive derivative or free acid.

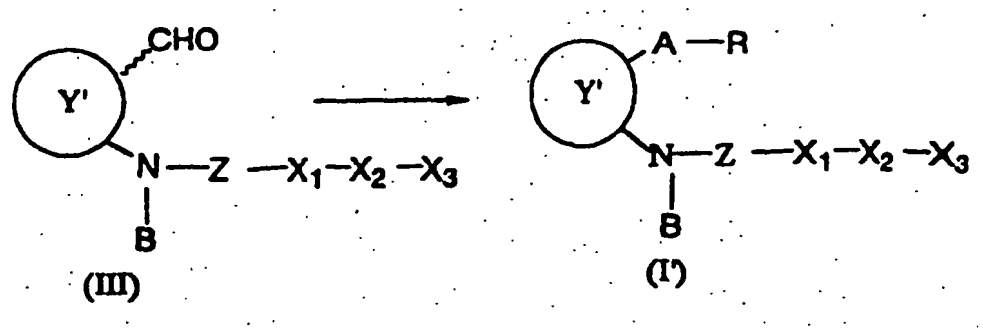
[0050] The reaction product can be purified by conventional purification methods, for example, the extraction with a solvent, chromatography, recrystallization, or the like.

[0051] Specific examples of the compound (II) as a starting material for the present method are as follows. -Examples of 3-amino[2.2.1]bicyclic compound include 7-(3-aminobicyclo[2.2.1]hept-2-yl)-5-heptenoic acid, 7-(3-aminobicyclo [2.2.1]hept-2-yl)-2,2-dimethyl-5-heptenoic acid, 7-(N-metnyl-3-aminobicyclo[2.2.1]hept-2-yl)-5-heptenoic acid, 6-(3-aminobicyclo[2.2.1]hept-2-yl)-5-hexenoic acid. Specific examples of 2-amino-6,6-dimethyl[3.1.1]bicyclic compound include 7-(2-amino-6,6-dimethylbicyclo[3.1.1]hept-3-yl)-5-heptenoic acid. In these starting compounds, the heptenoic acid chain may be saturated to form heptanoic acid chain, intervened by a hetero atom(s) or a hetero group(s) such as -O-, -S-, -NH-, or a phenylene(s), or substituted with an oxo group. Examples of such compounds include 7-(3-aminobicyclo [2.2.1]hept-2-yl)heptanoic acid, 4-[2-(2-aminobicyclo[3.1.1]hept-3-yl)ethoxyphenylacetic acid, 7-(3-aminobicyclo[2.2.1] hept-2-yl)-6-oxo-heptanoic acid. These starting compounds are either described in the Japanese Patent Publication No. JP 63-139161 or JP 01-52751, or can be prepared according to the method described therein.

[0052] Carboxylic acid $X_3\text{-}X_2\text{-}X_1\text{-}COOH$ corresponding to the partial structure $Z\text{-}X_1\text{-}X_2\text{-}X_3$ mean a carboxylic acid having substituents corresponding to the Xs above. That is, examples include alkane -carboxylic acid, alkene- carboxylic acid, alkyne-carboxylic acid, cycloalkane-carboxylic acid, cycloalkene carboxylic acid, aryl- carboxylic acid, aralkyloxy-carboxylic acid, heterocyclic-substituted-carboxylic acid, heteroarylalkyl-carboxylic acid, and substituted-amino- carboxylic acid. Each of the carboxylic acids may have a substituent (s) above. These carboxylic acids are commercially available or can be easily synthesized from a known compound(s) in accordance with a known method. Upon reaction, the carboxylic acid can be converted into the corresponding reactive derivative above, if necessary. For example, when an acid halide is needed, the compound is reacted with thionyl halide (e.g., thionyl chloride), phosphorous halide (e.g., phosphorous trichloride, phosphorous pentachloride) or oxalyl halide (e.g., oxalyl chloride) in accordance with a known

method such as those described in the literature (e.g., Shin-Jikken-Kagaku-Koza, vol. 14, pp. 1787 (1978), Synthesis, 852-854 (1986); Shin-Jikken-Kagaku-Koza, vol. 22, pp. 115 (1992)). The other reactive derivatives can also be prepared in accordance with known methods.

[0053] Among the objective compounds (Ib), those wherein the side chain A contains an unsaturated bond, especially a double bond, can also be prepared by reacting an aldehyde derivative of the general formula (III) below with an ylide compound corresponding to the rest of the side chain A-R under the conditions of the Wittig reaction:



wherein A, B, R, X_1, X_2, X_3, Y are as defined above, and Z is -CO-.

[0054] The starting compound (III) can be prepared in accordance with a method described in, for example, Japanese Patent Publication No. JP 02-256650. Further, an ylide compound corresponding to the rest of the side chain A-R can be synthesized by reacting triphanylphosphine with a corresponding halogenated alkanoic acid, or an ester derivative, ether derivative or amide derivative thereof in the presence of a base according to a known method.

[0055] Among the objective compounds (Ib), those wherein R is COOH can be converted into a corresponding ester derivative, alcohol derivative, ether derivative, amide derivative, if desired. For example, ester derivatives can be prepared by esterifying a carboxylic acid in a conventional manner. An ester derivative, when reduced, gives an alcohol derivative, and amidated, gives an amide derivative. An ether derivative can be obtained by O-alkylating an alcohol derivative.

[0056] The compound (Ib) of the present invention shows antagonistic effect against PGD_2 in vitro through the binding to PGD_2 receptor, and is useful as a drug for treating diseases in which mast cell dysfunction due to excessive production of PGD_2 is involved. For example, the compound (Ib) is useful as a drug for treating diseases, such as systemic mastocytosis and disorder of systemic mast cell activation, and also tracheal contraction, asthma, allergic rhinitis, allergic conjunctivitis, urticaria, injury due to ischemic reperfusion, and inflammation. The compound (Ib) shows preventive effect on nasal occlusion in vivo, and therefore is especially useful as a drug for treating that.

[0057] When using a compound (Ib) of the present invention in treatment, it can be formulated into ordinary formulations for oral and parenteral administration. A pharmaceutical composition containing a compound (Ib) of the present invention can be in the form for oral and parenteral administration. Specifically, it can be formulated into formulations for oral administration such as tablets, capsules, granules, powders, syrup, and the like; those for parenteral administration such as injectable solutions or suspensions for intravenous, intramuscular or subcutaneous injection, inhalant, eye drops, nasal drops, suppositories, or percutaneous formulations such as ointments.

[0058] In preparing the formulations, carriers, excipients, solvents, and bases known to one ordinary skilled in the art may be used. In case of tablets, they are prepared by compressing or formulating an active ingredient together with auxiliary components. Examples of usable auxiliary components include pharmaceatically acceptable excipients such as binders (e.g., cornstarch), fillers (e.g., lactose, microcrystalline cellulose), disintegrants (e.g., starch sodium glycolate) or lubricants (e.g., magnesium stearate). Tablets may be coated appropriately. In the case of liquid formulations such as syrups, solutions, or suspensions, they may contain suspending agents (e.g., methyl cellulose), emulsifiers (e.g., lecithin), preservatives, and the like. In the case of injectable formulations, it may be in the form of solution or suspension, or oily or aqueous emulsion, which may contain suspension-stabilizing agent or dispensing agent, and the like. In the case of an inhalant, it is formulated into a liquid formulation applicable to an inhaler. In the case of eye drops, it is formulated into a solution or a suspension. Especially, in the case of nasal drug for treating nasal occlusion, it can be used as a solution or suspension prepared by a conventional formulating method, or as a powder formulated using a powdering agent (e.g., hydroxypropyl cellulose, carbopole), which are administered into the nasal cavity. Alternatively, it can be used as an aerosol after filling into a special container together with a solvent of low boiling point.

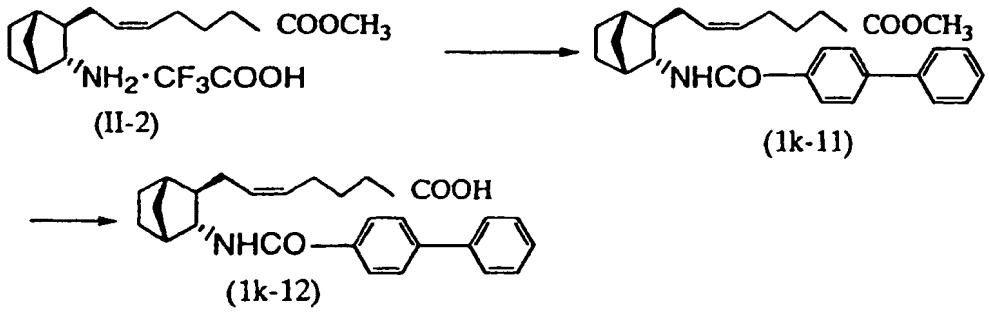
[0059] Although an appropriate dosage of the compound (Ib) varies depending on the administration route, age, body weight, sex, or condition of the patient, and the kind of drug(s) used together, if any, and should be determined by the physician in the end, in the case of oral administration, the daily dosage can generally be between about 0.01 - 100 mg, preferably about 0.01 - 10 mg, more preferably about 0.1 - 10 mg, per kg body weight. In the case of parenteral

administration, the daily dosage can generally be between about 0.001 - 100 mg, preferably about 0.001 - 1 mg, more preferably about 0.01 - 1 mg, per kg body weight. The daily dosage can be administered in 1 - 4 divisions.

[0060] The following Examples are provided to further illustrate the present invention and are not to be construed as limiting the scope thereof.

Example 1

[0061]

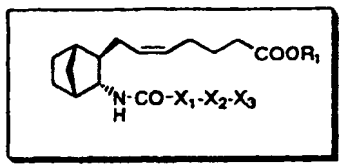


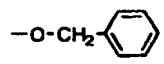
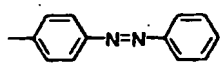
[0062] Methyl (Z)-7-[(1S,2R,3R,4R)-3-aminobicyclo[2.2.1]hept-2-yl]-5-heptenoate trifrluroroacetate (II-2) (232 mg, 0.636 mmol), which was prepared by the method described in Reference Example 4 of the Japanese Patent Publication No. JP 63-139161, was dissolved in methylene chloride (5 ml). To the solution were added triethylamine (0.279 ml, 2.00 mmol) and 4-biphenylcarbonyl chloride under ice-cooling and stirred for 7 hr at the same temperature. The reaction mixture was purified by column chromatography on silica gel (ethyl acetate/n-hexane (1:4)) to yield methyl (Z)-7-[(1S, 2R,3R,4R)-3-(4-biphenyl)carbonylaminobicyclo[2.2.1]hept-2-yl]-5-heptenoate (1k-11) (221 mg, 0.512 mmol). The compound (1k-11) (190 mg, 0.440 mmol) was dissolved in methanol (6ml). To the solution was added 1 N KOH (1.10 ml, 1.10 mmol) under ice-cooling and stirred for 15 hr at room temperature. The reaction mixture was concentrated in vacuo. The residue, after the addition of water (20 ml) and 1 N HCl (2 ml), was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous sodium sulfate and concentrated. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane (1:1) containing 0.3 % acetic acid) to yield (Z)-7-[(1S,2R, 3R,4R)-3-(4-biphenyl)carbonylaminobicyclo[2.2.1]hept-2-yl]-5-heptenoic acid (1k-12) (172 mg, 0.412 mmol). Yield 94 %.

[0063] The following compounds can also be prepared in the following manner.

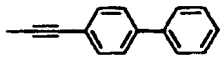
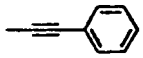
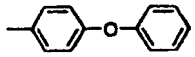
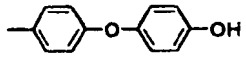
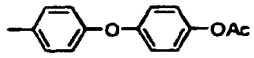
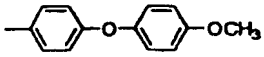
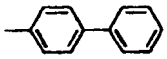
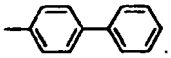
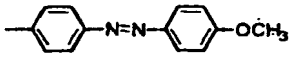
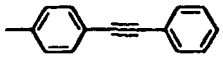
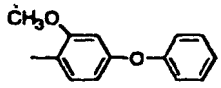
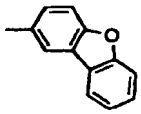
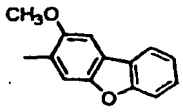
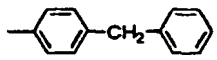
[0064] Compounds prepared in accordance with a method described in the Example above are shown in Tables below.

Table 1k



No.	R_1	X_1-X_2-X_3
1k-1	H	
1k-2	CH_3	
1k-3	H	

(continued)

No.	R_1	X_1-X_2-X_3
1k-4	H	
1k-5	H	
1k-6	H	
1k-7	H	
1k-8	H	
1k-9	H	
1k-10	H	
1k-11	CH_3	
1k-12	H	
1k-13	H	
1k-14	H	
1k-15	H	
1k-16	H	
1k-17	H	
1k-18	H	

(continued)

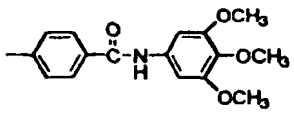
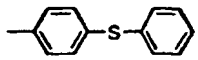
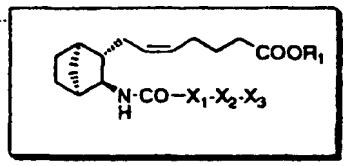
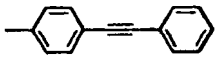
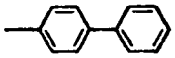
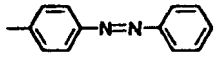
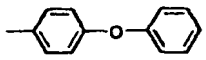
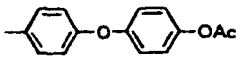
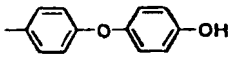
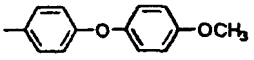
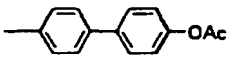
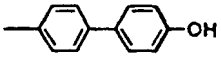
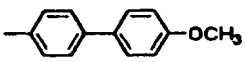
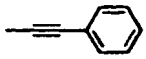
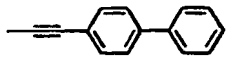
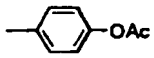
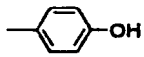
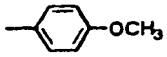
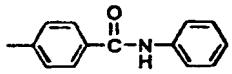
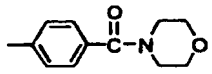
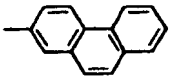
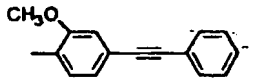
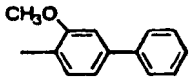
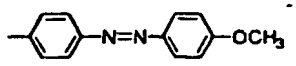
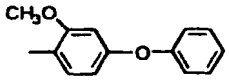
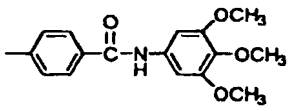
No.	R_1	X_1-X_2-X_3
1k-19	H	
1k-20	H	

Table 1m



No.	R_1	X_1-X_2-X_3
1m-1	CH_3	
1m-2	H	
1m-3	CH_3	
1m-4	H	
1m-5	CH_3	
1m-6	H	
1m-7	CH_3	
1m-8	H	
1m-9	CH_3	
1m-10	H	
1m-11	CH_3	
1m-12	H	
1m-13	CH_3	
1m-14	H	
1m-15	CH_3	
1m-16	H	
1m-17	CH_3	
1m-18	H	
1m-19	CH_3	

(continued)

No.	R_1	X_1-X_2-X_3
1m-20	H	
1m-21	H	
1m-22	H	
1m-23	CH_3	
1m-24	H	
1m-25	CH_3	
1m-26	H	
1m-27	CH_3	
1m-28	H	
1m-29	CH_3	
1m-30	H	
1m-31	H	
1m-32	H	
1m-33	H	
1m-34	H	
1m-35	H	
1m-36	H	
1m-37	H	
1m-38	H	

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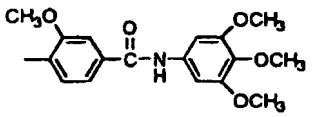
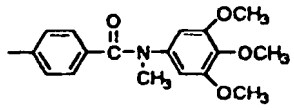
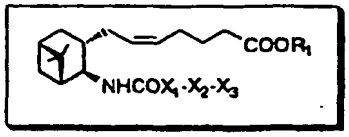
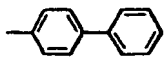
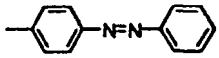
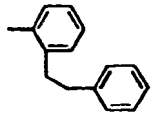
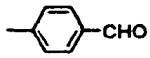
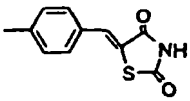
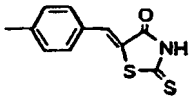
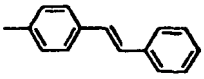
No.	R_1	X_1-X_2-X_3
1m-39	H	
1m-40	H	

Table 2a



No.	R_1	X_1-X_2-X_3
2a-1	CH_3	
2a-2	H	
2a-3	CH_3	
2a-4	H	
2a-5	Na	
2a-6	CH_3,	
2a-7	H	
2a-8	CH_3	
2a-9	H	
2a-10	CH_3	
2a-11	H	
2a-12	CH_3	
2a-13	H	
2a-14	CH_3	
2a-15	H	

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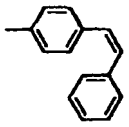
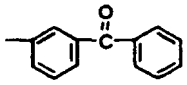
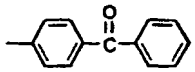
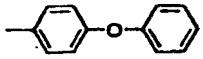
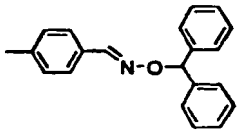
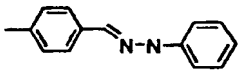
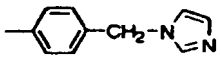
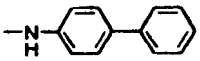
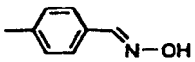
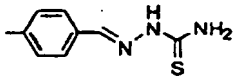
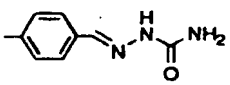
No.	R_1	X_1-X_2-X_3
2a-16	CH_3	
2a-17	H	
2a-18	CH_3	
2a-19	H	
2a-20	CH_3	
2a-21	H	
2a-22	Na	
2a-23	CH_3	
2a-24	H	
2a-25	CH_3	
2a-26	H	
2a-27	CH_3	
2a-28	H	
2a-29	CH_3	
2a-30	H	
2a-31	CH_3	
2a-32	CH_3	
2a-33	H	
2a-34	CH_3	
2a-35	H	
2a-36	CH_3	
2a-37	H	
2a-38	CH_3	
2a-39	H	
2a-40	CH_3	
2a-41	H	
2a-42	CH_3	
2a-43	H	

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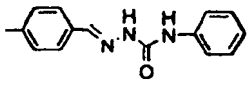
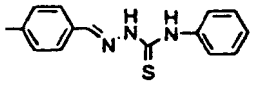
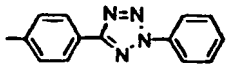
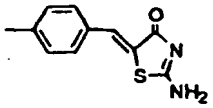
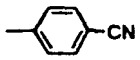
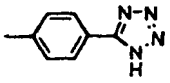
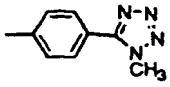
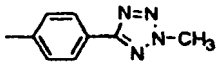
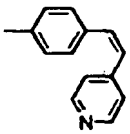
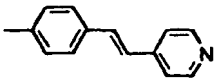
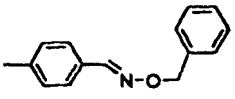
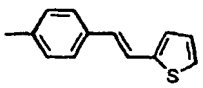
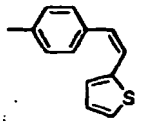
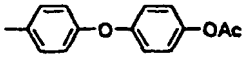
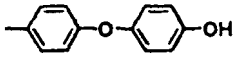
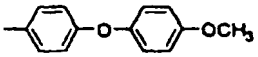
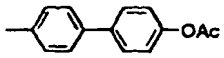
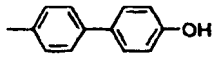
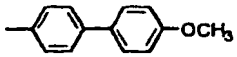
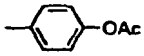
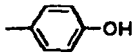
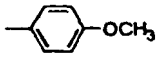
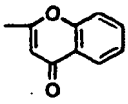
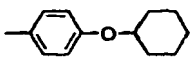
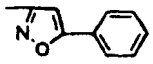
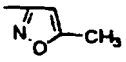
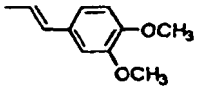
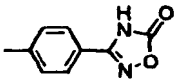
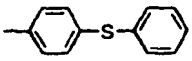
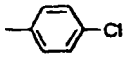
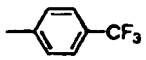
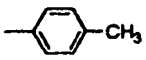
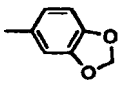
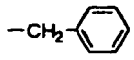
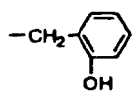
No.	R_1	X_1-X_2-X_3
2a-44	CH_3	
2a-45	H	
2a-46	CH_3	
2a-47	H	
2a-48	CH_3	
2a-49	H	
2a-50	CH_3	
2a-51	H	
2a-52	CH_3	
2a-53	H	
2a-54	CH_3	
2a-55	H	
2a-56	CH_3	
2a-57	H	
2a-58	CH_3	
2a-59	H	
2a-60	CH_3	
2a-61	H	
2a-62	CH_3	
2a-63	H	
2a-64	CH_3	
2a-65	H	
2a-66	CH_3	
2a-67	H	

(continued)

No.	R_1	X_1-X_2-X_3
2a-68	CH_3	
2a-69	H	
2a-70	CH_3	
2a-71	H	
2a-72	CH_3	
2a-73	H	
2a-74	CH_3	
2a-75	H	
2a-76	CH_3	
2a-77	H	
2a-78	CH_3	
2a-79	H	
2a-80	CH_3	
2a-81	H	
2a-82	CH_3	
2a-83	H	
2a-84	CH_3	
2a-85	H	
2a-86	CH_3	
		
2a-87	H	
2a-88	CH_3	
2a-89	H	
2a-90	CH_3	
2a-91	H	
2a-92	CH_3	
2a-93	H	
2a-94	CH_3	
2a-95	H	
2a-96	Na	
2a-97	$Ca^{1/2}$	
2a-98	CH_3	
2a-99	H	

(continued)

No.	R_1	X_1-X_2-X_3
2a-100	CH_3	
2a-101	H	
2a-102	CH_3	
2a-103	H	
2a-104	CH_3	
2a-105	H	
2a-106	CH_3	
2a-107	H	
2a-108	CH_3	
2a-109	H	
2a-110	Na	
2a-111	CH_3	
2a-112	H	
2a-113	CH_3	
2a-114	H	
2a-115	CH_3	
2a-116	H	
2a-117	CH_3	
2a-118	H	
2a-119	H	
2a-120	H	
2a-121	H	
2a-122	H	
2a-123	H	
2a-124	H	

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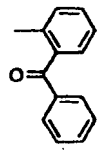
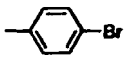
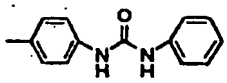
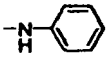
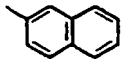
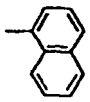
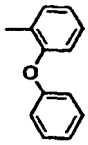
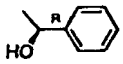
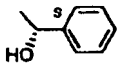
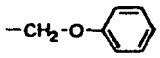
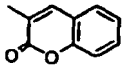
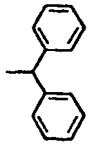
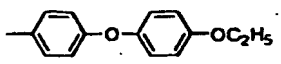
No.	R_1	X_1-X_2-X_3
2a-125	H	
2a-126	H	
2a-127	H	
2a-128	H	
2a-129	H	
2a-130	H	
2a-131	H	
2a-132	H	
2a-133	H	
2a-134	H	
2a-135	H	
2a-136	H	
2a-137	H	

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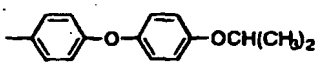
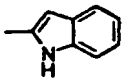
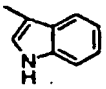
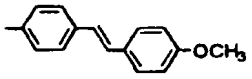
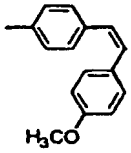
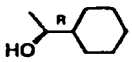
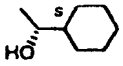
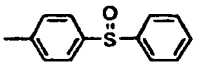
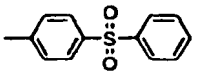
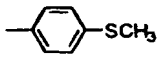
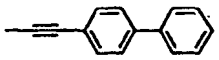
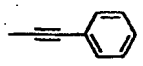
No.	R_1	X_1-X_2-X_3
2a-138	H	
2a-139	H	
2a-140	H	
2a-141	H	
2a-142	H	
2a-143	H	
2a-144	H	
2a-145	H	
2a-146	H	
2a-147	H	
2a-148	H	
2a-149	H	
2a-150	H	
2a-151	H	

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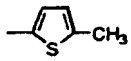
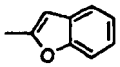
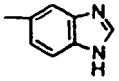
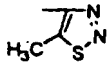
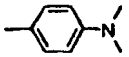
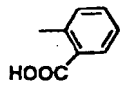
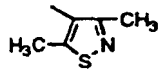
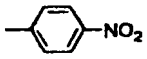
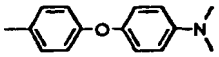
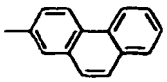
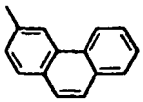
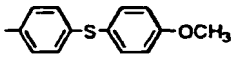
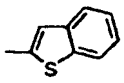
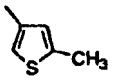
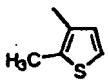
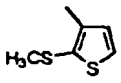
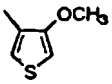
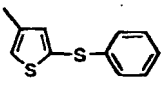
No.	R_1	X_1-X_2-X_3
2a-152	H	
2a-153	H	
2a-154	H	
2a-155	H	
2a-156	H	
2a-157	H	
2a-158	H	
2a-159	H	
2a-160	H	
2a-161	H	
2a-162	H	
2a-163	H	
2a-164	H	
2a-165	H	

(continued)

No.	R_1	X_1-X_2-X_3
2a-166	H	
2a-167	H	
2a-168	H	
2a-169	H	
2a-170	H	
2a-171	H	
2a-172	H	
2a-173	H	
2a-174	H	
2a-175	H	
2a-176	H	
2a-177	H	
2a-178	H	

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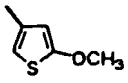
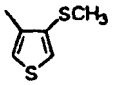
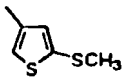
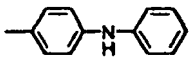
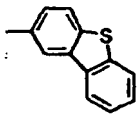
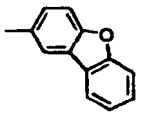
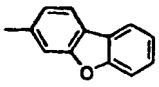
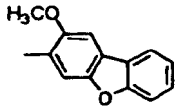
No.	R_1	X_1-X_2-X_3
2a-179	H	
2a-180	H	
2a-181	H	
2a-182	H	
2a-183	H	
2a-184	H	
2a-185	H	
2a-186	H	
2a-187	H	
2a-188	H	
2a-189	H	
2a-190	H	

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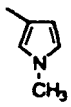
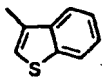
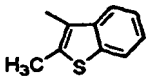
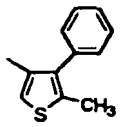
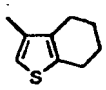
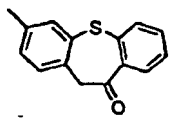
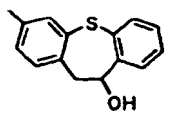
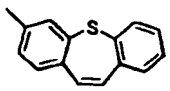
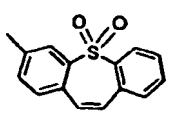
No.	R_1	X_1-X_2-X_3
2a-191	H	
2a-192	H	
2a-193	H	
2a-194	H	
2a-195	H	
2a-196	H	
2a-197	H	
2a-198	H	
2a-199	H	
2a-200	H	
2a-201	H	

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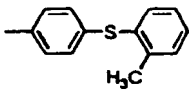
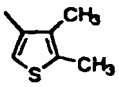
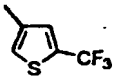
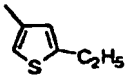
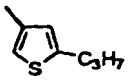
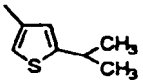
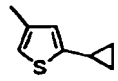
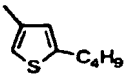
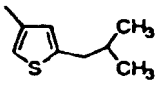
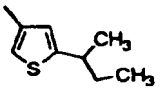
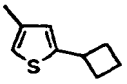
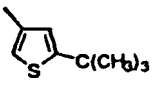
No.	R_1	X_1-X_2-X_3
2a-202	H	
2a-203	H	
2a-204		
2a-205		
2a-206		
2a-207		
2a-208		
2a-209		
2a-210		
2a-211		
2a-212		
2a-213		
2a-214		

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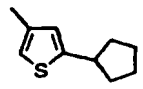
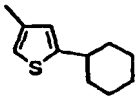
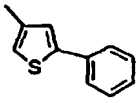
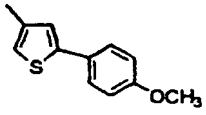
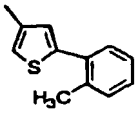
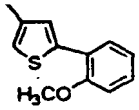
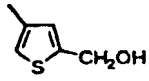
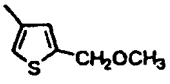
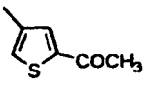
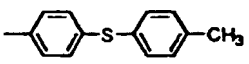
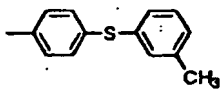
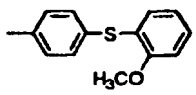
No.	R_1	X_1-X_2-X_3
2a-215		
2a-216		
2a-217		
2a-218		
2a-219		
2a-220		
2a-221		
2a-222		
2a-223		
2a-224		
2a-225		
2a-226		

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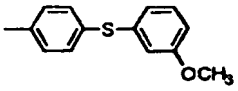
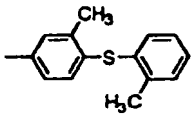
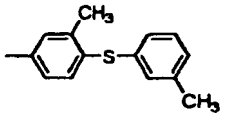
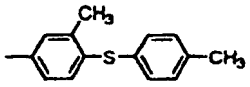
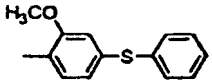
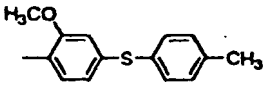
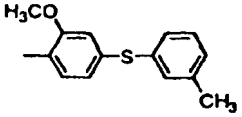
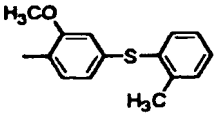
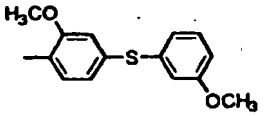
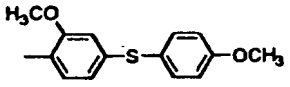
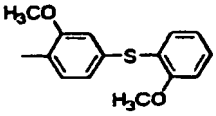
No.	R_1	X_1-X_2-X_3
2a-227		
2a-228		
2a-229		
2a-230		
2a-231		
2a-232		
2a-233		
2a-234		
2a-235		
2a-236		
2a-237		

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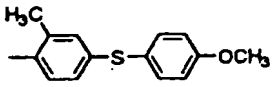
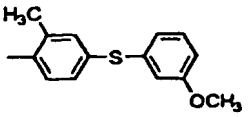
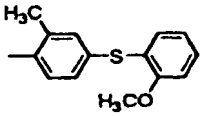
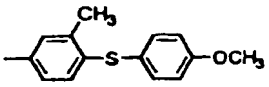
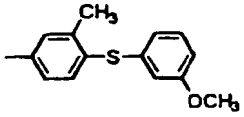
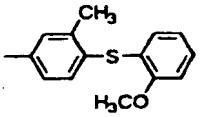
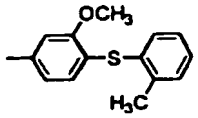
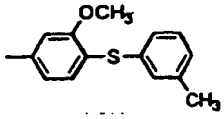
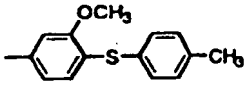
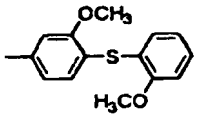
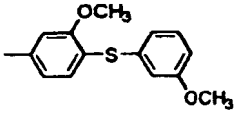
No.	R_1	X_1-X_2-X_3
2a-238		
2a-239		
2a-240		
2a-241		
2a-242		
2a-243		
2a-244		
2a-245		
2a-246		
2a-247		
2a-248		

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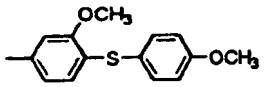
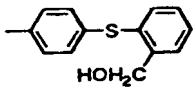
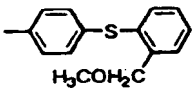
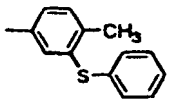
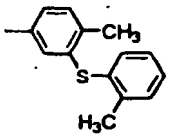
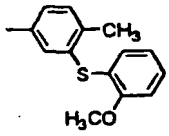
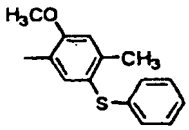
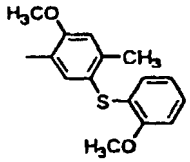
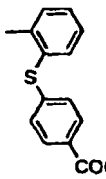
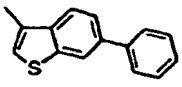
No.	R_1	X_1-X_2-X_3
2a-249		
2a-250		
2a-251		
2a-252		
2a-253		
2a-254		
2a-255		
2a-256		
2a-257		
2a-268		

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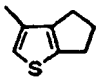
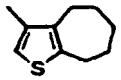
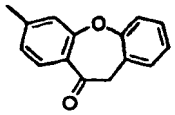
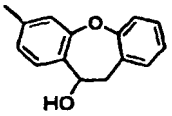
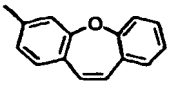
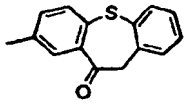
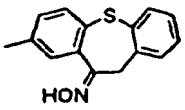
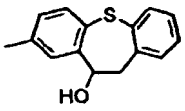
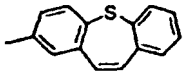
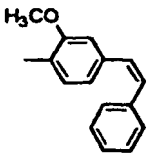
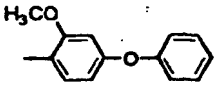
No.	R_1	X_1-X_2-X_3
2a-269		
2a-270		
2a-271		
2a-272		
2a-273		
2a-274		
2a-275		
2a-276		
2a-277		
2a-258		
2a-259		

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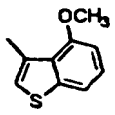
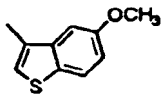
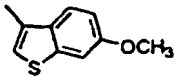
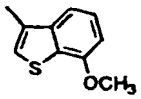
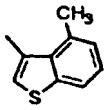
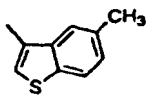
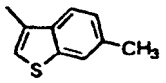
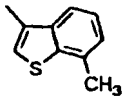
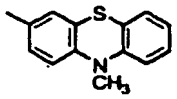
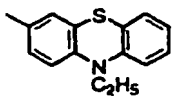
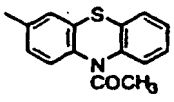
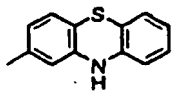
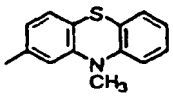
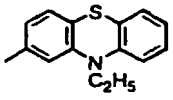
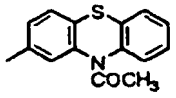
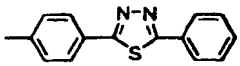
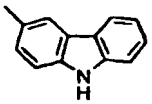
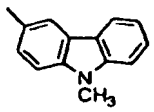
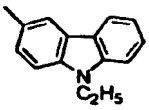
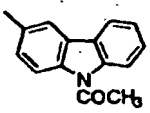
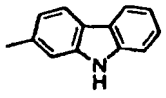
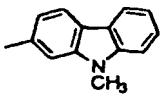
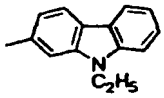
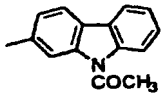
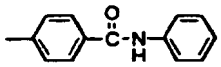
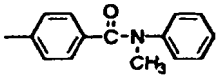
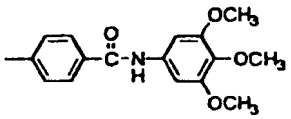
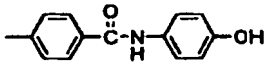
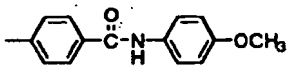
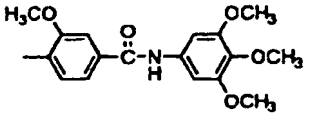
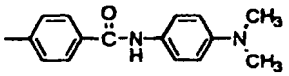
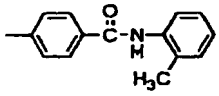
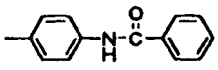
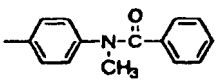
No.	R_1	X_1-X_2-X_3
2a-260		
2a-261		
2a-262		
2a-263		
2a-264		
2a-265		
2a-266		
2a-267		
2a-278		
2a-279		
2a-280		

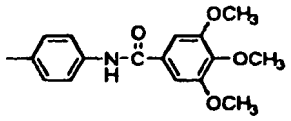
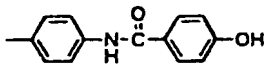
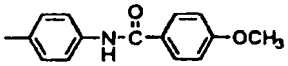
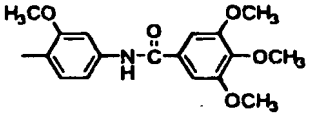
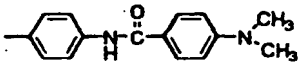
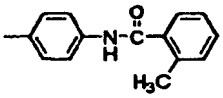
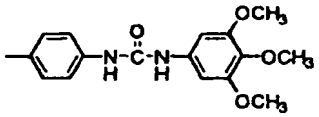
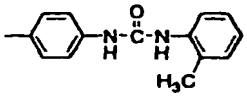
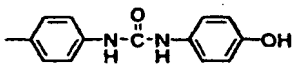
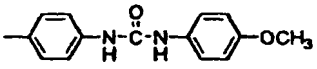
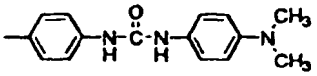
(continued)

No.	R_1	X_1-X_2-X_3
2a-281		
2a-282		
2a-283		
2a-284		
2a-285		
2a-286		
2a-287		
2a-288		
2a-289		
2a-290		
2a-291		

(continued)

No.	R_1	X_1-X_2-X_3
2a-292		
2a-293		
2a-294		
2a-295		
2a-296		
2a-197		
2a-298		
2a-299		
2a-300		
2a-301		
2a-302		
2a-303		

(continued)

No.	R_1	X_1-X_2-X_3
2a-304		
2a-305		
2a-306		
2a-307		
2a-308		
2a-309		
2a-310		
2a-311		
2a-312		
2a-313		
2a-314		

(continued)

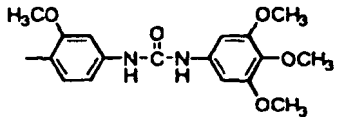
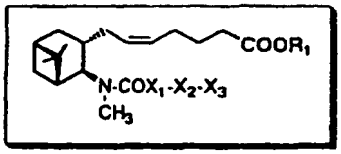
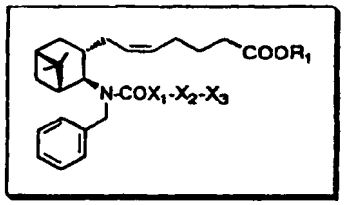
No.	R_1	X_1-X_2-X_3
2a-315		

Table 2b



No.	R_1	X_1-X_2-X_3
2b-1	H	
2b-2	H	

Table 2c



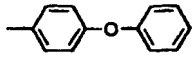
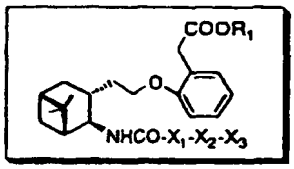
No.	R_1	X_1-X_2-X_3
2c-1	H	
2c-2	H	
2c-3	H	

Table 2d



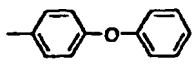
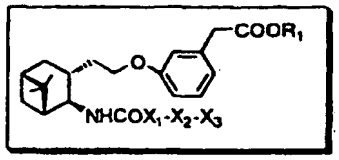
No.	R_1	X_1-X_2-X_3
2d-1	H	
2d-2	H	
2d-3	H	

Table 2e



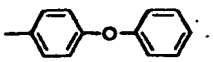
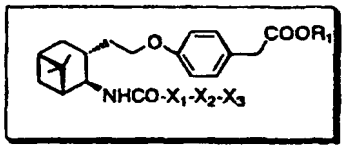
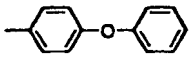
No.	R_1	X_1-X_2-X_3
2e-1	H	
2e-2	H	
2e-3	H	

Table 2f

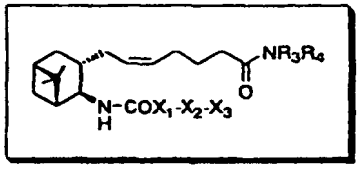


No.	R_1	X_1-X_2-X_3
2f-1	H	

(continued)

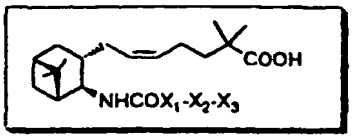
No.	R_1	X_1-X_2-X_3
2f-2	H	
2f-3	H	

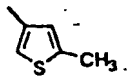
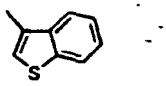
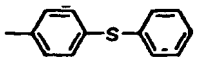
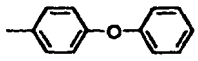
Table 2g



No.	R_3	R_4	X_1-X_2-X_3
2g-1	H	SO_2CH_3	

Table 2h



No.	X_1-X_2-X_3
2h-1	
2h-2	
2h-3	 
2h-4	
2h-5	

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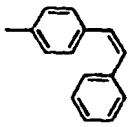
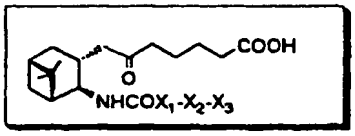
No.	X_1-X_2-X_3
2h-6	

Table 2i



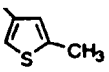
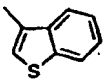
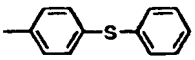
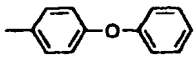
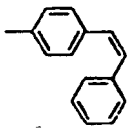
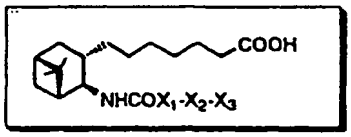
No.	X_1-X_2-X_3
2i-1	
2i-2	
2i-3	
2i-4	
2i-5	
2i-6	

Table 2j



(continued)

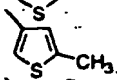
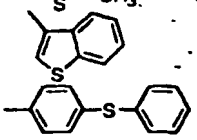
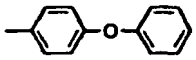
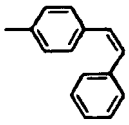
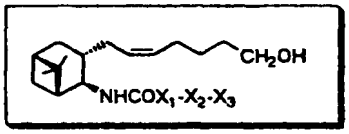
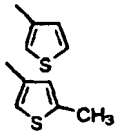
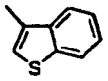
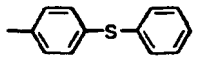
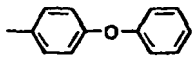
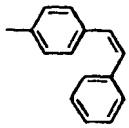
No.	X_1-X_2-X_3
2j-1	
2j-2	
2j-3	
2j-4	
2j-5	
2j-6	

Table 2k



No.	X_1-X_2-X_3
2k-1	
2k-2	
2k-3	
2k-4	
2k-5	
2k-6	

[0065] Physicochemical properties of compounds above are shown below. The compound number below corresponds

to that described in Tables above.

No.1k-1

[0066] $[\alpha]_D$= -25.4° ($CHCl_3$,c=1.08,23°C).

No.1k- 2

[0067] $CDCl_3$ 200MHz
1.07-2.28(14H,m),2.32(2H,t,J=7,4Hz),2.63(1H,m),3.63(3H,s),3.93(1H,m),5.3 °0-5.52(2H,m),6.35(1H,d,J=7.0Hz), 7.48-7.60(3H,m),7.88-8.02(6H,m). IR($CHCl_3$):3438,3002,2946,2868,1727,1652,1514,1485,1363,1310,1245,1154 /cm. $[\alpha]_D$=-80.4° ($CHCl_3$,c=1.01,24.0°C).

No.1k-3

[0068] $CDCl_3$ 200MHz
1.10-2.26(14H,m),2.37(2H,t,J=7.2Hz),2.60(1H,m),3.93(1H,m),5.30-5.50(2H, m), 6.33 (1H,d,J=7.5Hz), 7.48-7.58(3H, m), 7.88-7.99 (6H,m).
IR($CHCl_3$):3446,3004,2952,2874,1709,1652,1515,1485,1305,1153 /cm. $[\alpha]_D$=-96.4° ($CHCl_3$,c=1.05,23.0°C).

No.1k- 4

[0069] $CDCl_3$ 300MHz
1.05-2.17(14H,m),2.38(2H,t,J=7.2Hz),2.52(1H,m),3.81(1H,m),5.33-5.50(2H, m),6.08(1H,d,J=7.6Hz),7.39-7.53(3H,m), 7.57-7.62(6H,m). IR(CHCl3):3420,3250,3008,2948,2870, 2660,2208,1735(sh);1705,1640,1500/c m.
$[\alpha]_D$=-21.9±0.6° ($CHCl_3$,c=1.02,22°C).

No.lk-5

[0070] $CDCl_3$ 300MHz
1.05-2.14(14H,m),2.38(2H,t,J=7.2Hz),2.51(1H,m),3.81(1H,m),5.34-5.46(2H, m),6.07(1H,d,J=7.6Hz),7.33-7.56(SH,m).
IR($CHCl_3$):3422,3250,3010,2950,2876.2664,2558,2210,1735(sh),1705,1645,1 502,1441,1410,1307,1276/cm.
$[\alpha]_D$=-63.6± 1.9° ($CHCl_3$,c=0.56,22°C).

No.1k-6

[0071] $CDCl_3$ 300MHz
1.04-2.24(14H,m), 2.36(2H,t, J=7.5Hz), 2.58(1H,m), 3.88(1H,m), 5.30-5.43(2H, m), 6.21(1H, d,J=7.2Hz), 7.41-7.49(3H, m), 7.73-7.77(2H,m).
IR($CHCl_3$):3447,3011,2955,1708,1653,1603,1578,1515,1486,1457,1312,1211, 1164/cm.
$[\alpha]_D$=-60.3° ($CHCl_3$, c=1.00,23°C).

No.1k-7

[0072] $CDCl_3$ 300MHz
1.04-2.22(14H,m),2. 36(2H, t,J=7 .2Hz),2.57 (1 H,m), 3.87 (1 H,m),5.30-5.44(2H, m),6.17(1H,d,J=8.7Hz),6.99-7.40(7H, m),7.73(2H,d,J=7.5Hz).
IR($CHCl_3$):3449,3013,2955,1739,1708,1651,1609,1588,1522,1487,1243,1227, 1169/cm.
$[\alpha]_D$=-60.2° ($CHCl_3$,C=0.92,23°C).

No.1k-8

[0073] $CDCl_3$ 300MHz
1.04-2.25(14H,m),2.34(2H,t,J=7.5Hz),2.56(1H,m),3.87(1H,m),5.30-5.44(2H, m), 6.19 (1 H, d,J=7.5Hz).6.83-6.94 (6H, m), 7.69(2H, d,J=8.7Hz).
IR($CHCl_3$):3599,3455,3012,2955,1711,1644,1604,1577,1524,1507,1492,1290, 1236,1197,1170/cm.
$[\alpha]_D$=-47.7° ($CHCl_3$,c=1.01,22°C).

No.1k-9

[0074] $CDCl_3$ 300MHz
1.04-2.20(14H,m),2.31(3H,s),2.36(2H,t,J=7,2Hz),2.56(1H,m),3.86(1H,m),5.3 0-5.43(2H,m),6.16(1H,d,J=7.2Hz), 7.00-7.11(6H,m),7.74(2H,d,J=8.7Hz).
IR($CHCl_3$):3450,3010,2955,1750,1709,1651,1609,1596,1523,1489,1370,1247, 1227,1183/cm.
$[\alpha]_D$=-54.7° ($CHCl_3$,c=1.01,22°C).

No.1k-10

[0075] $CDCl_3$ 300MHz
1.04-2.22(14H,m),2.35(2H,t,J=7.2Hz),2.56(1H,m),3.82(3H,s),3.86(1H,m),5.3 0-5.43(2H,m),6.17(1H,d,J=6.9Hz), 6.89-7.01(6H,m),7.70(2H,d,J=8.7Hz).
IR($CHCl_3$):3023,2955,1742,1708,1649,1613,1602,1577,1522,1507,1490,1227, 1210,1170/cm.
$[\alpha]_D$=-58.1° ($CHCl_3$,C=1.01,22°C).

No.1m-1

[0076] $CDCl_3$ 300MHz
1.06-2.25(14H,m),2.32(2H,t,J=7.4Hz),2.61(1H,m),3.63(3H,s),3.91(1H,m),5.3 3-5.47(2H,m),6.24(1H,d,J=6.9Hz), 7.35-7.38(3H,m),7.53-7.60(4H,m),7.75-7.7 8(2H,m).
IR($CHCl_3$):3438,3008,2946,2875,2212,1732,1650,1605,1519,1496/cm.
$[\alpha]_D$= +76° ($CHCl_3$,c=1.39,24°C)

No.1m- 2

[0077] $CDCl_3$ 300MHz
1.05-2.20(14H,m),2.36(2H,t,J=6.2Hz),2.59(1H,m),3.89(1H,m),5.29-5.48(2H, m),6.26(1H,d,J=7.0Hz),7.26-7.38(3H,m), 7.52-7.60(4H,m),7.73-7.77(2H,m).
IR($CHCl_3$):3444,3012,2952,2874,2664,2214,1718(sh),1708,1649,1605,1520,1 498/cm.
$[\alpha]_D$= +81.4° ($CHCl_3$,c=1.01.23°C)

No.1m-3

[0078] $CDCl_3$ 300MHz 1.06-2.23(14H,m),2.32(2H,t,J=7.0Hz),2.62(1H,m),3.63(3H,s),3.93(1H,m),5.3 0-5.50(2H,m), 6.28(1H,d,J=7.0Hz), 7 .38-7.51(3H,m), 7 .58.-7.67(4H,m), 7.83-7.8 8(2H,m).
IR($CHCl_3$):3438,3008,2948,2875,1783(w), 1727,1650,1608,1580(w), 1523,150 1,14 82/cm .
$[\alpha]_D$= +59° ($CHCl_3$,c=1.49,25°C)

No.1m-4

[0079] $CDCl_3$ 300MHz
1.08-2.25(14H,m),2.36(2H,t,J=7.4Hz),2.59(1H,m),3.91(1H,m),5.28-5.48(3H, m),6.29(1H,d,J=7.4Hz),7.38-7.50(3H,m), 7.61-7.67(4H,m),7.81-7.86(2H,m).
IR($CHCl_3$):3436,3010,2948,2868,1727,1715(sh),1649,,16.15(w),1524,1502,14 82,1372/cm.
$[\alpha]_D$= +72° ($CHCl_3$,c=0.98,25°C)

No.1m- 5

[0080] $CDCl_3$ 300MHz
1.09-2.20(14H,m),2.32(2H,t,J=7.2Hz),2.63(1H,m),3.63(3H,s),3.92(1H,m),5.3 1-5.51(2H,m),6.35(1H,d,J=7.0Hz), 7.51-7.60(3H,m),7.92-7.97(6H,m).
IR($CHCl_3$):3436,3008,2946,2875,1727,1652,1608(w),1515,1484/cm.
$[\alpha]_D$= +82° ($CHCl_3$,c=0.99,25°C)

No.1m-6

[0081] $CDCl_3$ 300MHz

1.09-2.23(14H,m),2.37(2H,t,J=7.2Hz),2.60(1H,m),3.92(1H,m),5.30-5.49(2H, m),6.32(1H,d,J=7.4Hz),7.51-7.55(3H.m), 7.85-7.98(6H,m).
IR($CHCl_3$):3436,3010,2950,2875,2670,1727.1715(sh),1650,1605(w),1515,148 4/cm.
$[\alpha]_D$= +84° ($CHCl_3$,C=1.54,25°C)

No.1m-7

[0082] $CDCl_3$ 300MHz
1.03.2.18(14H,m).2.32(2H,t,J=7.4Hz),2.59(1H,m),3.64(3H,s),3.89(1H,m),5.2 9-5.49(2H,m),6.16(1H,d,J=7.8Hz), 6.98-7.06(4H,m),7.14-7.20(1H,m),7.34-7.4 1(2H,m),7.73-7.78(2H,m).
IR($CHCl_3$):3438,3008,2946,2868,1727,1648,1610,1586,1519,1485/cm.
$[\alpha]_D$= +54° ($CHCl_3$,c=1.29,25°C).

No.1m-8

[0083] $CDCl_3$ 300MHz
1.06-2.21(14H,m),2.36(2H,t,J=7.5Hz),2.58(1H,m),3.88(1H,m),5.31-5.46(2H, m),6.17(1H,d,J=6.9Hz),6.99-7.05(4H,m), 7.15-7.21(1H,m),7.36-7.41(2H,m),7. 72-7.75(2H,m).
IR($CHCl_3$):3436,3010,2948.2868,2675,1730(sh),1709,1647,1608,1586,1520,1 485/cm.
$[\alpha]_D$= +56° ($CHCl_3$,c=0.97,25°C)

No.1m-9

[0084] $CDCl_3$ 300MHz
1.05-2.18(14H,m),2.29-2.34(5H,m),2.59(1H,m),3.64(3H,s),3.89(1H,m),5.32-5. 46(2H,m),6.16(1H,d,J=7.5Hz), 7.00-7.11(6H,m),7.74-7.77(2H,m).
IR($CHCl_3$):3440,3010,2946,2868,1729,1649,1595,1519,1488/cm.
$[\alpha]_D$= +47° ($CHCl_3$,c=0.82,25°C).

No.1m-10

[0085] $CDCl_3$ 300MHz
1.04-2.20(14H,m),2.31-2.39(5H,m),2.57(1H,m),3.87(1H,m),5.28-5.47(2H,m), 6.17(1H, d,J=7.0Hz),6.99-7.12(6H,m), 7.72-7.76(2H,m).
IR($CHCl_3$):3674,3572,3438,3010,2948,2868,2626,1748,1710,1648,1615,1595, 1520,1489/cm..
$[\alpha]_D$= +51° ($CHCl_3$,c=0.91,25°C)

No.1m-11

[0086] $CDCl_3$ 300MHz
1.04-2.16(14H,m),2.31(2H,t,J=7.2Hz),2.59(1H,m),3.63(3H,s),3.89(1H,m),5.2 9-5.49(2H,m),6.24(1H,d,J=7.4Hz),6.54 (1H,s),6.83-6.93(6H,m),7.69-7.73(2H, m).
IR($CHCl_3$):3674,3588,3438,3296,3010,2946,2868,1725,1646,1603,1520,1504, 1489/cm.
$[\alpha]_D$= +51° ($CHCl_3$,c=0.91.25°C)

No.1m-12

[0087] $CDCl_3$ 300MHz
1.04-2.21(14H,m),2.33(2H,t,J=8.0Hz),2.56(1H,m),3.87(1H,m),5.28-5.48(2H, m),6.23(1H,d,J=8.0Hz),6.75(1H,m), 6.87-6.94(6H,m),7.66-7.71(2H,m),9.63(1 H,brs).
IR($CHCl_3$):3674,3582,3436,3275,3010,2950,2868,2675,1727,1710(sh),1643,1 603,1522,1504,1490/cm.
$[\alpha]_D$= +30° ($CHCl_3$,c=0.97,25°C)

No.1m- 13

[0088] $CDCl_3$ 300MHz
1.01-2.18(14H,m),2.31(2H,t.J=7.4Hz),2.58(1H,m),3.63(3H,s),3.82(3H,s),3.89 (1H,m),5.29-5.48(2H,m).6.14(1H,d, J=7.OHz),6.88-7.02(6H,m),7.70-7.74(2H, m).

IR($CHCl_3$):3442,3402,3004,2946,2868,1727,1648,1600,1518,1499/cm.
$[\alpha]_D$=+42° ($CHCl_3$,c=1.82,26°C)

No.1m-14

[0089] $CDCl_3$ 300MHz
1.05-2.21(14H,m),2.35(2H,t,J=7.2Hz),2.55(1H,m),3.82(3H,s),3.88(1H,m),5.2 7-5.46(2H,m),6.16(1H,d,J=7.2Hz), 6.88-7.02(6H,m),7.68-7.73(2H,m).
IR($CHCl_3$):3438,3012,2948,2870,2650,1730(sh),1709,1647,1615(sh),1601,15 19,1492/cm.
$[\alpha]_D$=+64° ($CHCl_3$,c=0.70,25°C)

No.1m-15

[0090] $CDCl_3$ 300MHz
1.05-2.20(14H,m),2.29-2.36(5H,m),2.62(1H,m),3.63(3H,s),3.92(1H,m),5.30-5. 50(2H,m),6.25(1H,d,J=7.2Hz), 7.16-7.21(2H,m),7.59-7.64(4H,m),7.83-7.87(2 H,m).
IR($CHCl_3$):3446,3010,2946,2868,1745(sh),1728,1650,1615,1525,1507,1486/c m.
$[\alpha]_D$=+65.0° ($CHCl_3$,c=1.02,23°C)

No.1m-16

[0091] $CDCl_3$ 300MHz
1.08-2.21(14H,m),2.34-2.40(5H,m),2.59(1H,m),3.90(1H,m),5.29-5.48(2H,m), 6.29(1H,d,J=7.OHz),7.18(2H,d, J=8.6Hz),7.58-7.64(4H,m),7.83(2H,d,J=8.2Hz).
IR($CHCl_3$):3438,3012,2948,2870,2622,1749,1710,1649,1610,1526,1508,1487/ cm.
$[\alpha]_D$=+66° ($CHCl_3$,c=1.21,24°C)

No.1m-17

[0092] $CDCl_3$ 300MHz
1.06-2.19(14H,m),2.32(2H,t,J=7.2Hz),2.62(1H,m),3.63(3H,s),3.93(1H,m),5.30-5.50(2H,m),6.32(1H,d,J=7.6Hz),6.41 (1H,s), 6.94(2H,d,J=9.0Hz), 7.47(2H,d, J=9.0Hz),7.58(2H,d,J=8.6Hz),7.81(2H,d,J=8.6Hz).
IR($CHCl_3$):3580,3434,3284,3010,2946,2868,1726,1646,1606,1528,1490/cm.
$[\alpha]_D$=+62.4° ($CHCl_3$,c=1.01,23°C)

No.1m- 18

[0093] $CDCl_3$+CD_3OD 300MHz
1.11-2.18(14H,m),2.32(2H,t,J=7.4Hz),2.59(1H,m),3.88(1H,m),5.30-5.49(2H, m),6.55(1H,d,J=7.0Hz),6.92(2H,d, J=8.6Hz),7.47(2H,d,J=8.6Hz),7.59(2H,d,J =8.6Hz),7.79(2H,d,J=8.2Hz).
IR(Nujol):3398,3175,2725,1696,1635,1601,1531,1510/cm.
$[\alpha]_D$=+99.5° (CH_3OH,c=1.011,25°C)

No.1m-19

[0094] $CDCl_3$ 300MHz
1.05-2.20(14H,m),2.32(2H,t,J=7.4Hz),2.61(1H,m),3.63(3H,s),3.86(3H,s),3.94 (1H,m),5.30-5.50(2H,m),6.24(1H,d, J=7.OHz),6.99(2H,d,J=8.6Hz),7.53-7.63(4 H,m),7.82(2H,d,J=8.6Hz).
IR($CHCl_3$):3440,3006,2946,2875,1726,1649,1606,1527,1510,1489/cm.
$[\alpha]_D$=+68° ($CHCl_3$,c=0.88,26°C)

No.1m - 20

[0095] $CDCl_3$ 300MHz
1.09-2.20(14H,m),2.35(2H,t,J=7.3Hz),2.58(1H,m),3.85(3H,s),3.89(1H,m),5.2 8-5.48(2H,m),6.35(1H,d,J=7.2Hz),6.98 (2H,d,J=8.8Hz),7.51-7.61(4H,m),7.81(2H,d,J=8.4Hz),8.34(1H,brs).
IR($CHCl_3$):3446,3012,2952,2881,2640,1730(sh),1707,1647,1606,1527,1510,1 489/cm.
$[\alpha]_D$=+83° ($CHCl_3$,c=1.00,25°C).

No.1m- 21

[0096] $CDCl_3$ 300MHz
1.05-2.14(14H,m),2.37(2H,t,J=7.2Hz),2.51(1H,m),3.81(1H,m),5.34-5.46(2H, m),6.11(1H,d,J=7.5Hz),7.33-7.48(3H,m), 7.53-7.55(2H,m).
IR($CHCl_3$):3420,3250,3008,2948,2870,2660,2210,1735(sh),1705,1645,1503,1 441,1409/cm.
$[\alpha]_D$=+59.2±1.0° ($CHCl_3$,c=1.023, 22°C).

No.1m - 22

[0097] $CDCl_3$ 300MHz
1.05-2.17(14H, m), 2.37(2H, t,J=7.2Hz), 2.52(1H,m), 3.82(1H,m), 5.32-5.47(2H, m),6.20(1H,d,J=7.6Hz),7.38-7.53(3H, m),7.58-7.61(6H,m),9.11(1H,brs).
IR($CHCl_3$):3420,3250,3010,2984,2870,2675,2208,1730(sh),1705,1640,1500,1 406/cm.
$[\alpha]_D$=+57.4° ($CHCl_3$,c=1.83.23°C).

No.1m- 23

[0098] $CDCl_3$ 300MHz
1.05-2.18(14H,m),2.31(2H,t,J=7.5Hz),2.60(1H,m),3.63(3H,s),3.90(1H,m),5.3 2-5.47(2H,m),6.22(1H,d,J=6.9Hz), 7.40-7.49(3H,m),7.76-7.79(2H,m).
IR($CHCl_3$):3438,3008,2946,2868,1727,1651,1603,1585,1512,1484/cm.
$[\alpha]_D$=+52° ($CHCl_3$,c=1.49,25°C).

No.1m- 24

[0099] $CDCl_3$ 300MHz
1.05-2.21(14H,m),2.36(2H,t,J=7.2Hz),2.57(1H,m),3.89(1H,m),5.28-5.47(2H, m),6.22(1H,d,J=7.0Hz),7.39-7.55(3H,m), 7.73-7.79(2H,m).
IR($CHCl_3$):3676,3572,3436,3010,2948,2875,1730(sh),1709,1650,1600,1580,1 514,1484/cm.
$[\alpha]_D$=+57° ($CHCl_3$,c=0.97,26°C).

No.1m- 25

[0100] $CDCl_3$ 300MHz
1.04-2.18(14H,m),2.28-2.35(5H,m),2.59(1H,m),3.62(3H,s),3.88(1H,m),5.29-5. 49(2H,m),6.20(1H,d,J=7.2Hz),7.15(2H, d,J=9.0Hz),7.80(2H,d,J=8.8Hz).
IR($CHCl_3$):3436,3010,2946,2868,1752,1727,1653,1602,1519,1491/cm.
$[\alpha]_D$=+53° ($CHCl_3$,c=1.63,25°C).

No.1m- 26

[0101] $CDCl_3$ 300MHz
1.05-2.19(14H,m), 2.32-2.38(5H,m), 2.56(1H,m), 3.88(1H,m), 5.29-5.47(2H,m), 6.25(1H,d,J=7.4Hz), 7.15(2H,d, J=9.0Hz), 7.78(2H,d,J=8.6Hz).
IR($CHCl_3$):3434,3016,3006,2948,2880,2622,1752,1730(sh),1710,1651,1605,1 520,1492/cm.
$[\alpha]_D$=+58° ($CHCl_3$,c=3.68,24°C)

No.1m - 27

[0102] $CDCl_3$ 300MHz
1.05-2.16(14H,m).2.30(2H.t,J=7.5Hz).2.57(1H,m).3.62(3H,s),3.87(1H,m).5.2 7-5.47(2H,m),6.32(1H,d,J=7.4Hz),6.85 (2H,d,J=8.6Hz),7.62(2H,d,J=8.6Hz),8. 35(1H,s
IR($CHCl_3$):3580,3450,3216,3010,2946,2868,1726,1640,1608,1584,1528,14961 cm.
$[\alpha]_D$=+56.2° ($CHCl_3$,c=0.713,23°C)

No.1m- 28

[0103] $CDCl_3$ 200MHz
1.10-2.25(14H,m),2.32(2H,t,J=7.2Hz),2.55(1H,brs),3.82-3.93(1H,m),5.27-5.4 7(2H,m), 6.25(1H,d,J=7.4Hz), 6.86(2H,d, J=8.6Hz), 7.62(2H,d,J=8.6Hz).
IR($CHCl_3$):3438,3242,2675,1730(sh),1708,1639,1607,1585/cm.

No.1m-29

[0104] $CDCl_3$ 300MHz
1.05-2.18(14H,m), 2.31(2H, t,J=7.4Hz), 2.58(1H,m), 3.64(3H,s), 3.85(3H,s), 3.89 (1H,m),5.29-5.48(2H,m),6.14(1H,d, J=6.6Hz),6.92(2H,d,J=9.0Hz),7.74(2H,d, J=9.0Hz).
IR($CHCl_3$):3445,3008,2946,2868,1727,1646,1606,1578,1623,1493/cm.
$[\alpha]_D$=+53° ($CHCl_3$,c=2.03,24°C)

No.1m-30

[0105] $CDCl_3$ 300MHz
1.04-2.21(14H,m),2.36(2H,t,J=7.3Hz),2.56(1H,m),3.85(3H,s),3.88(1H,m),5. 27-5.46(2H,m),6.15(1H,d,J=7.2Hz),6.92 (2H,d,J=8.6Hz),7.73(2H,d,J=8.6Hz)
IR($CHCl_3$):3440,3010,2950,2870,2645,1727,1710(sh),1646,1606,1575,1524,1 494/cm.
$[\alpha]_D$=+62° ($CHCl_3$,c=1.10,24°C).

No.1m-31

[0106] $CDCl_3$+CD_3OD 300MHz
1.16-2.20(14H,m),2.31(2H,t, J=7.2Hz),2.59(1H,m),3.85(1H,m),5.31-5.51(2H, m),7.13-7.21(1H,m),7.31-7.42(2H,m), 7.68-7.93(6H,m).
IR(Nujol):3344,3175,2715,2675,1699,1631,1566/cm.
$[\alpha]_D$=+67° (CH_3OH,c=1.01,24°C).

No.1m-32

[0107] $CDCl_3$ 200MHz
1.09-2.23(14H,m),2.33(2H,t,J=7.1Hz),2.57(1H,brs),3.40-3.93(9H,m),4.41(1H, brs),5.29-5.48(2H.m).6.44(1H.d, J=7.4Hz).7.43(2H,d.J=8.2Hz),7.80(2H,d,J=7. 8Hz).
IR($CHCl_3$):3434,3354,1726,1720(sh),1660(sh),1626/cm.

No.1m-33

[0108] $CDCl_3$ 200MHz
1.14-2.25(14H,m),2.37(2H,t,J=7.3Hz),2.64(1H,brs),3.93-4.01(1H,m),5.30-5.5 1(2H,m),6.47(1H,d,J=7.4Hz),7.63-7.74 (2H,m),7.79(2H,s),7.89-7.93(1H,m),8. 00(1H,dd,J=2.3,1.0Hz).8.30(1H,d,J=1.0Hz),8.65-8.73(2H,m).
IR($CHCl_3$):3450,2675,1728,1707,1649,1528,1509/cm.
$[\alpha]_D$=+82.8±1.2° ($CHCl_3$,c=1.01,23°C).

No.2a-1

[0109] $[\alpha]_D$=+69.0° (MeOH,c=1.01,25°C)

No.2a-2

[0110] $CDCl_3$ 300MHz
0.99(1H,d,J=10.2Hz),1.15 and 1.24(each 3H,each s),1.50.2.50(14H,m),4.3 0(1H,m),5.35-5.52(2H,m),6.32(1H,d, J=8.7Hz),7.36-7.49(3H,m),7.58-7.62(2H, m),7.66 and 7.80(each 2H,each d,J=8.7Hz).
IR($CHCl_3$):3116,3014,2925,2870,2663,1708,1651,1610,1524,1504,1484,1472 /cm.
$[\alpha]_D$= +64.1° (MeOH,c=1.02,25°C).

No.2a-3

[0111] $[\alpha]_D$=+76.6° (MeOH,c=1.18,26°C).

No.2a-4

[0112] $CDCl_3$ 300MHz
0.99(1H,d,J=10.2Hz),1.15 and 1.25(each 3H,each s),1.64.2.51(14H,m),4.3 1(1H,m),5.36-5.53(2H,m),6.33(1H,d, J=8.4z),7.50-7.56(3H,m),1,85-7.98(6H, m).
IR($CHCl_3$):3515,3452,3014.2925.2870,1740.1708,1654,1517.1486,1470 /cm.
$[\alpha]_D$= +79.5° (MeOH,c=1.18, 22°C).

No.2a-5

[0113] CD_3OD 300MHz
0.98(1H,d,J=9.9Hz),1.18 and 1.25(each 3H,each s),1.56-1.71(3H,m),1.98-2. 40(11H,m),4.17(1H,m),5.41-5.52(2H,m), 7.52-7.61(3H,m),7.91-8.01(6H,m).
IR(KBr):3416,3063,2983,2921,2869,1704,1643,1566,1518,1488,1408 /cm.
$[\alpha]_D$= +62.0° (MeOH,c=1.00, 25°C).

No.2a-6

[0114] $[\alpha]_D$=+64.1° (MeOH,c=1.01,25°C).

No.2a-7

[0115] $[\alpha]_D$=+65.3° (MeOH,c=0.99,25°C).

No.2a-8

[0116] $[\alpha]_D$=+74.0° (MeOH,c= 1.01,25°C).

No.2a-9

[0117] $[\alpha]_D$=+71.0° (MeOH,c=1.10,25°C).

No.2a-10

[0118] $[\alpha]_D$=+74.7° (MeOH,c=1.00,25°C).

No.2a-11

[0119] $[\alpha]_D$=+72.1° (MeOH,c=1.00,25°C).

No.2a-12

[0120] $[\alpha]_D$=+53.1° ($CHCl_3$,c=1.01,26°C).
m.p.155.0-156.0°C

No.2a-13

[0121] $CDCl_3$ 300MHz
0.98(1H,d,J=10.2Hz),1.18 and 1.25(each 3H,each s),1.63-2.40(14H,m),4.3 0(1H,m),5.46-5.58(2H,m),6.44(1H,d, J=8.4Hz),7.49 and 7.77(each 2H,each d,J=8.7Hz),7.54(1H,s).
IR($CHCl_3$):3689,3378,3028,3014,2924,1713,1652,1602,1522,1496 /cm.
$[\alpha]_D$= +78.3° (MeOH,c=0.84,25°C).
m.p.205.0-206.0°C

No.2a-14

[0122] $[\alpha]_D$=+72.5° (MeOH,c=1.07,25°C).

No.2a-15

[0123] $CDCl_3$ 300MHz
0.99(1H,d,J=9.9Hz),1.14 and 1.24(each 3H,each s),1.55.2.44(14H,m),4.27(1H,m),5.30-5.50(2H,m),6.29(1H,d, J=9.0Hz),7.11 and 7.20(each 1H,each d, J=16.2Hz),7.29-7.55(5H,m),7.57 and 7.72(each 2H,each d,J=8.7Hz).
IR($CHCl_3$):3453,3083,3022,3013,2925,2870,1708,1650,1607,1560,1522,1496 /cm.
$[\alpha]_D$= +72.3° (MeOH,c=1.00,27°C).
m.p.115.0-117.0°C

No.2a-16

[0124] $CDCl_3$ 300MHz
0.92(1H,d,J=10.2Hz),1.11 and 1.23(each 3H, each s),1.50-2.48(14H,m),3.6 2(3H,s),4.29(1H,m),5.30-5.50(2H,m),6.20 (1H,d,J=8.7Hz),6.59 and 6.68 (each 1H, each, d,J=12.3Hz), 7.23(5H,s), 7.29 and 7.59(each 2H, each d,J=8. 1Hz).
IR($CHCl_3$):3453,3024,3016,2924,2870,1730,1651,1607,1520,1495 /cm.
$[\alpha]_D$= +56.8° (MeOH,c=1.04,24°C).

No.2a-17

[0125] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.11 and 1.23(each 3H,each s), 1.50-2.38(14H,m),4.2 6(1H,m),5.30-5.50(2H,m), 6.23(1H,d, J=8.4Hz), 6.59 and 6.70(each 1H, each d,J=12.3Hz), 7.23(5H,s), 7.30 and 7.57(each 2H,each d,J=8.7Hz).
IR($CHCl_3$):3452,3081,3019,3014,2925,2870,2665,1708,1650,1607,1521,1495 /cm.
$[\alpha]_D$= +61.6° (MeOH,c=1.00, 27°C).

No.2a-18

[0126] $CDCl_3$ 300MHz
0.97(1H, d, J=10.2Hz), 1.11 and 1.23(each 3H, each, s), 1.50-2.50(14H, m), 3.61 (3H,s), 4.31(1H,m), 5.35-5.51(2H,m), 6.33(1H,d,J=8.4Hz), 7.48-7.64(4H,m), 7.7 9-7.83(2H,m), 7.91(1H, dt, J=1.5 and 7.8Hz), 8.01(1H, dt, J=1.5 and 7.8Hz), 8. 13(1H, t, J=1.5Hz).
IR($CHCl_3$):3450,3026,3013,29Z5,2870,1730,1659,1600,1510 /cm.
$[\alpha]_D$= +56.0° (MeOH,c=1.01,25°C).

No.2a-19

[0127] $CDCl_3$ 300MHz
0.95(1H,d,J=9.9Hz),1.14 and 1.21(each 3H,each s),1.53-2.60(14H,m),4.25(1H,m),5.35-5.64(2H,m),7.21(1H,d, J=7.8Hz),7.49-7.68(4H,m),7.76-7.84(3H,m),8.25(1H,m),8.43(1H,m).
IR($CHCl_3$):3382,3196,3025,3015,2925,2870,1725,1652,1599,1577,1521 /cm.
$[\alpha]_D$= +55.9° (MeOH,c=1.00,25°C).

No.2a-20

[0128] $CDCl_3$ 300MHz
0.98(1H,d,J=10.2Hz),1.13 and 1.24(each 3H,each s),1.50-2.50(14H,m),3.6 2(3H,s),4.31(1H,m),5.35-5.51(2H,m),6.24 (1H,d,J=8.4Hz),7.40-7.52(3H,m),7. 71-7.76(2H,m).
IR($CHCl_3$):3453,3025,3013,2925,2870,1730,1753,1579,1514,1486 /cm.
$[\alpha]_D$= +61.2° (MeOH,c=1.04,25°C).

No.2a-21

[0129] $CDCl_3$ 300MHz
0.98(1H,d,J=10.2Hz),1.13 and 1.23(each 3H,each s),1.52-2.50(14H,m),4.2 8(1H,m),5.34-5.51(2H,m),6.27(1H,d,

J=8.7Hz),7.41-7.53(3H,m),7.71-7.74(2H, m).
IR($CHCl_3$):3452,3063,3027,3014,2925,2871,1708,1652,1578,1515,1486 /cm.
$[\alpha]_D$= +62.0° (MeOH,c=1.01,27°C).

No.2a-22

[0130] d_6-DMSO 300MHz
0.86(1H,d,J=9.9Hz), 1.10 and 1.16(each 3H,each s),1.42-1.52(3H,m),1.85-2. 46(11H,m), 3.98(1H,m),5.32-5.43(2H,m), 7.41(3H.m),7.88(2H,d,J=6.6Hz),8.19 (1H,d,J=6.6Hz).
IR(KBr):3367,3060,2984,2922,2868,1634,1563,1529,1487/cm.
$[\alpha]_D$=+47.7° (MeOH,c=1.00,25°C).

No.2a-23

[0131] $[\alpha]_D$=+62.7° (MeOH,c=1.01,27°C).

No.2a-24

[0132] $CDCl_3$ 300MHz
0.99(1H,d,J=10.2Hz),1.14 and 1.25(each 3H,each s),1.52-2.50(14H,m),4.3 1(1H,m),5.36-5.52(2H,m),6.34(1H,d, J=8.4Hz),7.47-7.52(2H,m),7.59-7.64(1H, m), 7.78-7.83(6H,m).
IR($CHCl_3$):3449,3027,3013,2925,2869,1708,1656,1599,1518,1493 /cm.
$[\alpha]_D$= +63.1° (MeOH,c=1.00,25°C).

No.2a.25

[0133] $[\alpha]_D$=+35.1° (MeOH,c=1.00,25°C).

No.2a-26

[0134] $[\alpha]_D$=+35.5° (MeOH,c=1.02,25°C).

No.2a-27

[0135] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.12 and 1.23(each 3H,each s),1.52-2.50(14H, m),3.6 3(3H,s),4.29(1H,m),5.36-5.51(2H,m),6.18 (1H,d,J=8.4Hz),7.01 and 7.71 (each 2H,each d,J=8.7Hz,),6.98-7.05(2H,m),7.16(1H,t,J=7.5Hz),7.34-7.41(2 H,m).
IR($CHCl_3$):3455,3024,3016,2924,2870,1730,1651,1588,1520,1487 /cm. $[\alpha]_D$=+56.4° (MeOH,c=1.01,25°C).

No.2a.28

[0136] $CDCl_3$ 300MHz
0.98(1H,d,J=10.2Hz),1.12 and 1.23(each 3H,each s),1.52-2.50(14H,m),4.2 6(1H,m),5.34-5.51(2H,m),6.20(1H,d, J=9.0Hz),7.01 and 7.70(each 2H, each d,J=9.0Hz,),6.98-7.15(2H,m),7.17(1H,t,J=7.5Hz),7.34-7.40(2H,m).
IR($CHCl_3$):3454, 3031, 3018, 2925, 2870,1708,1650,1588,1523,1487/cm.
$[\alpha]_D$= +56.2° (MeOH,c=1.00,25°C).

No.2a-29

[0137] $[\alpha]_D$=+53.0° (MeOH,c=1.03,25°C).

No.2a-30

[0138] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.10 and 1.23(each 3H,each s),1.52-2.50(14H,m),4.2 5(1H,m),5.30-5.50(2H,m),6.23(1H,d, J=8.7Hz),6.36(1H,s),7.26-7.39(10H,m),7. 60 and 7.68(each 2H,each d,J=8.4Hz,).
IR($CHCl_3$):3451,3088,3064,3029,3014,2925,2869,1707,1652,1522,1495 /cm.
$[\alpha]_D$=+54.2° (MeOH,c=1.00,25°C).

No.2a-31

[0139] $CDCl_3$ 300MHz
0.98(1H,d,J=10.2Hz),1.14 and 1.24(each 3H,each s),1.50-2.50(14H,m),3.6 3(3H,s),4.31(1H,m),5.30-5.50(2H,m),6.26 (1H,d,J=8.4Hz),6.90(1H,t,J=7.4Hz), 7.13(1H,d,J=8.7Hz),7.29(2H,t,J=8.0Hz),7.67-7.75(5H,m),7.82(1H,s).
IR(Nujol):3380,3244,1723,1638,1601,1578,1535,1495 /cm.
$[\alpha]_D$=+73.6° (MeOH,c=0.50,26°C).
m.p.133.0-134.0°C

No.2a.32

[0140] $[\alpha]_D$=+56.1° (MeOH,c=1.02,26°C).

No.2a-33

[0141] $CDCl_3$ 300MHz
0.95(1H,d,J=10.2Hz),1.10 and 1.21(each,3H,each s),1.50-2.50(14H,m),4.25 (1H,m),5.13(2H,s),5.30-5.70(3H,m),6.41 (1H, d,J=8.2Hz),6.89 (1H, s); 7.09(1H, s),7.17 and 7.72(each 2H,each d,J=8.2Hz),7.62(1H,s).
IR($CHCl_3$):3450,3125,3031,3013,2925,2870,2467,1917,1708,1654,1615,1575, 1523,1497 /cm.
$[\alpha]_D$=+55.2° (MeOH,c=1.01,26°C).

No.2a-34

[0142] $[\alpha]_D$=+72.9° (MeOH,c=1.03,25°C).

No.2a-35

[0143] $CDCl_3$ 300MHz
0.98(1H,d,J=10.2Hz),1.13 and 1.24(each 3H,each s),1.52-2.48(l4H,m),4.2 8(1H,m),5.35.5.51(2H.m).6.28 (1H.d.J=8.7Hz),7.34-7.37(3H.m),7.52-7.55(2H, m),7.58 and 7.71(each 2H,each d,J=8.7Hz).
IR($CHCl_3$):3515,3452,3030,3012,2925,2870,1739,1708,1652,1607,1555,1521, 1497 /cm.
$[\alpha]_D$=+74.3° (MeOH,c=1.01,25°C).

No.2a-36

[0144] $[\alpha]_D$=+23.4° (MeOH,c=1.07,25°C).

No.2a-37

[0145] $CDCl_3$ 300MHz
0.83(1H,d,J=10.5Hz),0.95 and 1.18(each 3H,each s),1.44-2.46(14H,m),3.9 2(1H,m),5.34-5.52(3H,m),7.26-7.54(9H,m), 7.62(1H,s).
IR($CHCl_3$):3432,3310,3189,3023,3014,2924,2870,1704,1610,1594,1523,1487 /cm.
$[\alpha]_D$=+25.3° (MeOH,c=1.00,26°C).

No.2a-38

[0146] $[\alpha]_D$=+70.9° (MeOH,c=1.02,25°C).

No.2a.39

[0147] $[\alpha]_D$=+70.6° (MeOH,c=1.01,25°C).

No.2a-40

[0148] $[\alpha]_D$=+74.7° (MeOH,c=1.00,25°C).

No.2a-41

[0149] $[\alpha]_D$=+72.1° (MeOH,c=1.01,24°C).

No.2a.42

[0150] $[\alpha]_D$=+69.2° (MeOH,c=1.00,25°C).

No.2a.43

[0151] $[\alpha]_D$=+70.8° (MeOH,c=1.00,25°C).

No.2a-44

[0152] $[\alpha]_D$=+60.4° (MeOH,c=1.00,26°C).

No.2a-45

[0153] $CDCl_3$ 300MHz
0.97(1H,d,J=9.9Hz),1.13 and 1.23(each 3H,each s),1.55-2.52(14H,m),4.29(1H,m),5.34-5.54(2H,m),6.33(1H,d, J=9.0Hz),7.10(1H,t,J=7.4Hz),7.34(2H,t,J =7.4Hz),7.52(2H,m),7.68 and 7.75(each 2H,each d,J=8.4Hz),7.80(1H,s),8 10 (1H,s),10.09(1H,s).
IR($CHCl_3$):3393,3195,3093,3033,3013,2925,2870,1698,1656,1598,1537,1498 /cm .
$[\alpha]_D$=+59.4° (MeOH,c=1.01,24°C).

No.2a-46

[0154] $[\alpha]_D$=+63.5° (MeOH,c=1.00,25°C).

No.2a-47

[0155] $CDCl_3$ 300MHz
0.97(1H,d,J=9.9Hz),1.12 and 1.23(each 3H,each s),1.54-2.48(14H,m),4.29(1H,m),5.35-5.52(2H,m),6.32(1H,d, J=8.7Hz),7.26(1H,m),7.41(2H,t,J=7.8Hz), 7.64(2H,d,J=7.5Hz),7.73 and 7.77(each 2H,each d,J=8.4Hz),7.95(1H,s),9. 20(1H,s),10.38(1H,s).
IR($CHCl_3$):3450,3339,3003,2992,2925,2870,1706,1653,1596,1523,1495/cm.
$[\alpha]_D$=+63.3° (MeOH,c=1.00,25°C).

No.2a.48

[0156] $[\alpha]_D$=+63.8° (MeOH,c=1.00,24°C).

No.2a.49

[0157] $CDCl_3$ 300MHz
1.00(1H,d,J=10.5Hz),1.17 and 1.26(each 3H,each s).1.55-2.52(14H.m).4.3 4(1H,m),5.36-5.54(2H,m),6.35(1H.d, J=9.0Hz),7.50-7.62(3H,m),7.90 and 8.3 3(each 2H,each d,J=8.4Hz).8.21(2H,m)
IR($CHCl_3$):3451,3029,3022,3016,2925,2870,1708,1655,1542,1508,1498,1471, 1459 /cm.
$[\alpha]_D$=+63.5° (MeOH,c=1.02,25°C):
m.p.135.0-137.0 °C

No.2a-50

[0158] $[\alpha]_D$=+68.9° (MeOH,c=1.01,24°C).

No.2a-51

[0159] d_6-DMSO 300MHz

0.87(1H,d,J=9.9Hz),1.10 and 1.17(each 3H,each s),1.40-1.60(3H,m),1.90-2. 40(11H,m), 3.98(1H,m), 5.35-5.46(2H,m), 7.64(1H,s), 7.65 and 7.91(each 2H, each d,J=8.7Hz), 8.06(1H,d,J=6.0Hz), 9.32(1H, brs).
IR(KBr):3385, 2962, 1734, 1707, 1632, 1529, 1498 /cm.
$[\alpha]_D$=+68.4° (MeOH,c=1.01,24°C).

No.2a-52

[0160] $[\alpha]_D$=+76.2° (MeOH,c=1.01,24°C).

No.2a-53

[0161] $[\alpha]_D$=+73.9° (MeOH,c=1.02,24°C).

No.2a-54

[0162] $[\alpha]_D$=+68.1° (MeOH,c=1.00,24°C).

No.2a.55

[0163] $[\alpha]_D$=+67.8° (MeOH,c=1.00,24°C).

No.2a-56

[0164] $[\alpha]_D$=+65.4° (MeOH,c=1.03,25°C).

No.2a-57

[0165] $[\alpha]_D$=+63.4° (MeOH,c=1.01,24°C).

No.2a-58

[0166] $[\alpha]_D$=+66.6° (MeOH,c=1.01,24°C).

No.2a.59

[0167] $[\alpha]_D$=+65.5° (MeOH,c=1.00,24°C).

No.2a.60

[0168] $[\alpha]_D$=+60.9° (MeOH,c=1.02,25-C).

No.2a-61

[0169] $CDCl_3$ 300MHz
0.97(1H,d,J=IO.OHz),1.10 and 1.22(each 3H,each s),1.50-2.50(14H,m),4.2 6(1H,m),5.30-5.54(2H,m),6.28(1H,d, J=8.6Hz),6.60 and 6.82(each 1H,each d,J=12.4Hz),7.12(2H,d,J=6.0Hz),7.25 and 7.62(each 2H,each d,J=8.6Hz),8.47 (2H,d,J=6.OHz).
IR($CHCl_3$):3452,3027,3019,3013,2925,2870,2980,1708,1651,1606,1520,1494 /cm.
$[\alpha]_D$=+61.6° (MeOH,c=1.01,25°C).

No.2a.62

[0170] $[\alpha]_D$=+72.0° (MeOH,c=0.93,25°C).

No.2a-63

[0171] $CDCl_3$ 300MHz
0.99(1H,d,J=10.2Hz),1.14 and 1.24(each 3H,each s),1.50-2.50(14H,m),4.2 9(1H,m),5.36-5.55(2H,m),6.35(1H,d,

J=9.1Hz),7.04 and 7.27(each 1H,each d,J=16.5Hz),7.37(2H,d,J=6.6Hz),7.56 and 7.76(each 2H,each d,J=8.4Hz), 8.57 (2H,d,J=6.6Hz).
IR($CHCl_3$):3452,3024,3018,3014,2925,2870,2470,1933,1708,1.652,1605,1521, 1496 /cm.
$[\alpha]_D$=+69.2° (MeOH,c=1.01,25°C).

No.2a-64

[0172] $[\alpha]_D$=+56.9° (MeOH,c=1.24,25°C).

No.2a-65

[0173] $CDCl_3$ 300MHz
0.98(1H,d,J=10.5Hz),1.12 and 1.23(each 3H,each s),1.54-2.46(14H,m),4.2 7(1H,m),5.23(2H,s),5.34-5.52(2H,m),6-.26 (1H,d,J=8.4Hz),7.32-7.45(5H,m),7. 64 and 7.71(each 2H,each d,J=8.4Hz),8.15(1H,s).
IR($CHCl_3$):3452,3088,3065,3032,3013,2925,2870,1708,1653,1611,1559,1522, 1496 /cm.
$[\alpha]_D$=+61.0° (MeOH,c=0.91,25°C).

No.2a-66

[0174] $[\alpha]_D$=+76.0° (MeOH,c=1.01,25°C).

No.2a-67

[0175] $CDCl_3$ 300MHz
0.98(1H,d,J=10.4Hz),1.14 and 1.24(each 3H, each s), 1.54-2.46(14H,m),4.2 8(1H,m), 5.32-5.53(2H,m), 6.27(1H,d, J=8.6Hz), 6.92-7.31(each 1H, each d,J= 16.4Hz), 7.02(1H,dd,J=5.8 and 3.6Hz), 7.12(1H,d,J=3.6Hz), 7.24(1H,d,J=5.8 Hz),7.51 and 7.70(each 2H, each d,J=8.4Hz).
IR($CHCl_3$):3453,3029,3013,2925,2870,1739, 1650,1604,1524,1515,1494 /cm.
$[\alpha]_D$=+76.2° (MeOH,c=1.00,24°C).
m.p.104.0-106.0°C

No.2a-68

[0176] $[\alpha]_D$=+57.7° (MeOH,c=1.01,25°C).

No.2a-69

[0177] $CDCl_3$ 300MHz
0.99(1H,d,J=10.2Hz),1.14 and 1.24(each 3H,each s),1.54-2.48(14H,m),4.2 8(1H, m),5.34-5.53(2H, m),6.29(1H,d, J=9.0Hz),6,54-6.74(each 1H, each d,J= 12.OHz),7.02(1H,dd,J=4.8 and 3.3Hz),6.97(1H,dd,J=3.3 and 1.2Hz),7.13(1 H, dd,J=4.8 and 1.2Hz),7.44 and 7.70(each 2H, each d,J=8.7Hz).
IR($CHCl_3$):3453,3025,3010,2925,2870,1708,1650,1607,1559,1523,1493 /cm.
$[\alpha]_D$=+58.4° (MeOH,c=1.00,25°C).

No.2a-70

[0178] $[\alpha]_D$=+48.6° (MeOH,c=1.00,25°C).

No.2a-71

[0179] $CDCl_3$ 300MHz
0.98(1H,d,J=10.2Hz),1.12 and 1.23(each 3H,each s),1.52-2.46(14H,m),2.3 1(3H,s),4.26(1H,m),5.33-5.52(2H,m),6.20 (1H,d,J=9.3Hz),7.02-7.11(6H,m),7. 70(2H,d,J=9.0Hz).
IR($CHCl_3$):3460.3031.3022,3011.2925.2870.1750,1708.1650,1608,1597,1523, 1490 /cm.
$[\alpha]_D$=+48.9° (MeOH,c=1.01,25°C).

No.2a-72

[0180] $[\alpha]_D$=+51.2° (MeOH,c=1.02,25°C).

No.2a.73

[0181] $CDCl_3$ 300MHz
0.97(1H,d,J=9.9Hz),1.11 and 1.23(each 3H,each s),1.54.2.48(14H.m).4.27(1H,m),5.32-5.52(2H,m),6.24(1H,d, J=9.0Hz),6.83-6.94(6H,m),7.65(2H,d,J=9. 0Hz).
IR($CHCl_3$):3598,3451,3199,3033,3012,2925,2870,1708,1642,1604,1524,1507, 1491 /cm.
$[\alpha]_D$=+52.2° (MeOH,c=1.01,25°C).

No.2a-74

[0182] $[\alpha]_D$=+51.5° (MeOH,c=0.92,25°C).

No.2a-75

[0183] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.11 and 1.23(each 3H,each s),1.55-2.46(14H,m),3.8 2(3H,s),4.25(1H,m),5.32-5.52(2H,m),6.19 (1H,d,J=8.7Hz),6.89-7.01(6H,m),7. 65-7.68(2H,m).
IR($CHCl_3$):3450,3025,3008,2925,2870,2837,1741,1649,1612,1521,1505,1490 /cm.
$[\alpha]_D$=+51.1° (MeOH,c=1.00,25°C).

No.2a-76

[0184] $[\alpha]_D$=+60.4° (MeOH,c=0.98,25°C).

No.2a-77

[0185] $CDCl_3$ 300MHz .
0.99(1H,d,J=10.5Hz),1.15 and 1.24(each 3H,each s),1.54-2.48(14H,m),2.3 4(3H,s),4.29(1H,m),5.32-5.54(2H,m),6.32 (1H,d,J=8.4Hz),7.19 and 7.60 (each 2H,each d,J=8.4Hz),7.63 and 7.79(each 2H,each d,J=8.4Hz).
IR($CHCl_3$):3452,3027,3012,2925,2870,1751,1709,1651,1611,1560,1527,1509, 1489 /cm.
$[\alpha]_D$=+61.2° (MeOH,c=1.00,25°C).

No.2a-78

[0186] $[\alpha]_D$=+67.4° (MeOH,c=1.01,25°C).

No.2a-79

[0187] $CDCl_3$ 300MHz
0.99(1H,d,J=10.2Hz),1.15 and 1.24(each 3H,each s),1.54.2.54(14H,m),4.3 1(1H,m),5.32-5.54(2H,m),6.36(1H,d, J=8.2Hz),6.93 and 7.48(each 2H,each d,J=8.6Hz),7.59 and 7.75(each 2H,each d,J=8.4Hz).
IR($CHCl_3$):3593,3448,3192,3030,3010,2925,2870,1708,1644,1608,1591,1559, 1530,1516,1491 /cm.
$[\alpha]_D$=+65.8° (MeOH,c=1.01,25°C).

No.2a-80

[0188] $[\alpha]_D$=+66.9° (MeOH,c=1.01,25°C).

No.2a-81

[0189] $CDCl_3$ 300MHz
0.99(1H,d,J=10.5Hz),1.15 and 1.24(each 3H,each s),1.54-2.48(14H,m),3.8 6(3H,s),4.29(1H,m),5.34-5.52(2H,m),6.20 (1H,d,J=8.7Hz),6.99 and 7.55 (each 2H,each d,J=9.0Hz),7.61 and 7.77(each 2H,each d,J=8.7Hz).
IR($CHCl_3$):3450,3009.2925.2870.2838,1740.1708.1650.1608.1557.1528,1512. 1491 /cm.

$[\alpha]_D$=+66.2° (MeOH,c=1.01,25°C).

No.2a-82

[0190] $[\alpha]_D$=+57.7° (MeOH,c=1.02,24°C).

No.2a-83

[0191] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.12 and, 1.23(each 3H,each s),1.54-2.48(14H,m),2.3 3(3H,s),4.26(1H,m),5.32-5.52(2H,m),6.25 (1H,d,J=8.7Hz),7.16 and 7.75 (each 2H,each d,J=8.7Hz).
IR($CHCl_3$):3452,3030,3022,3012,2925,2870,1754,1709,1654,1604,1585,1522, 1493 /cm.
$[\alpha]_D$=+57.4° (MeOH,c=1.01,24°C).

No.2a-84

[0192] $[\alpha]_D$=+57.8° (MeOH,c=1.01,24°C).

No.2a-85

[0193] $CDCl_3$ 300MHz
0.95(1H,d,J=10.2Hz),1.12 and 1.22(each 3H,each s),1.54-2.48(1.4H,m),4.2 5(1H,m),5.32-5.52(2H,m),6.280H,d, J=8.7Hz),6.87 and 7.57(each 2H,each d,J=9.0Hz).
IR($CHCl_3$):3590,3450,3166.3019,3012,2925,2871.1708,1637,1608,1583,1531, 1498 /cm.
$[\alpha]_D$=+56.0° (MeOH,c=1.01,24°C).

No.2a.86

[0194] $[\alpha]_D$=+59.3° (MeOH,c=1.01,22°C).

No.2a-87

[0195] $CDCl_3$ 300MHz
0.98(1H,d,J=10.0Hz),1.13 and 1.23(each 3H,each s), 1.54-2.48(14H,m), 3.8 5(3H,s), 4.25(1H,m), 5.32-5.53(2H,m), 6.19(1H,d,J=8.8Hz), 6.93 and 7.69 (each 2H,each d,J=9.0Hz).
IR($CHCl_3$):3450,3030,3017,3012,2925,2870,2840,1740,1708,1647,1606,1575, 1525,1496 /cm.
$[\alpha]_D$=+58.2° (MeOH,c=0.99,22°C).

No.2a-88

[0196] $[\alpha]_D$=+50.9° (MeOH,c=1.02,25°C).

No.2a-89

[0197] $CDCl_3$ 300MHz
0.99(1H,d,J=10.2Hz),1.18 and 1.26(each 3H,each s),1.56-2.48(l4H,m),4.2 9(1H,m),5.36-5.54(2H,m),7.03(1H,d, J=8.7Hz),7.21(1H,s),7.43(2H,m),7.74(1 H,ddd,J=1.8,6.9 and 8.7Hz),8.22(1H,dd,J=1.8 and 8.1Hz).
IR($CHCl_3$):3443,3087,3023,3014,2925,2870,1708,1685,1658,1630,1517,1466 /cm .
$[\alpha]_D$=+57.1° (MeOH,c=1.01,22°C).
m.p.117.0-118.0°C

No.2a.90

[0198] $[\alpha]_D$=+54.1° (MeOH,c=1.01,22°C).

No.2a.91

[0199] $CDCl_3$ 300MHz

0.97(1H,d.J=10.2Hz),1.13 and 1.23(each 3H,each s),1.52-2.46(14H,m),4.2 4(1H,m),5.34-5.52(2H,m),6.49-6.53(12H, m),7.11(1H,dd,J=0.9 and 3.6Hz),7.4 4(1H,dd,J=0.9 and 1.8Hz).
IR($CHCl_3$):3437,3033,3022,3014,2925,2870,1739,1708,1655,1595,1520,1472 /cm.
$[\alpha]_D$=+55.0° (MeOH,c=1.00,22°C).

No.2a-92

[0200] $[\alpha]_D$=+50.3° (MeOH,c=1.00,22°C).

No.2a-93

[0201] $CDCl_3$ 300MHz
0.95(1H,d,J=10.5Hz), 1.12 and 1.23(each 3H,each s),1.52-2.46(14H,m),4.2 5(1H,m), 5.34-5.52(2H,m), 6.12(1H,d, J=8.7Hz), 7.07(1H,dd,J=3.9 and 5.1Hz), 7.45-7.48(2H,m).
IR($CHCl_3$):3450,3023,3011,2925,2870,1739,1708,1645,1531,1501,1471 /cm.
$[\alpha]_D$=+49.1° (MeOH,c=1.02,24°C).

No.2a-94

[0202] $[\alpha]_D$=+51.5° (MeOH,c=1.00,24°C).

No.2a.95

[0203] $CDCl_3$ 300MHz
0.96(1H,d,J=10.5Hz),1.11 and 1.23(each 3H,each s),1.52-2.46(14H,m),4.2 5(1H,m),5.34-5.56(2H,m),6.14(1H,d, J=8.7Hz),7.34(2H,d,J=2.0Hz),7.85(1H,t, J=2.0Hz).
IR($CHCl_3$):3452,3114,3030,3013 2925,2870,1708,1649,1535,1498,1471/cm.
$[\alpha]_D$=+55.5° (MeOH,c=1.00,25°C).
m.p.87.0-88.0°C

No.2a-96

[0204] CD_3OD 300MHz
0.94(1H,d,J=10.2Hz),1.13 and 1.22(each 3H,each s),1.50-1.76(3H,m),I.94-2.39(11H,m),4.11(1H,m),5.39-5.49(2H, m), 7.43-7.51(2H,m),8.05(1H,m).
IR(KBr):3369,3084,2985,2921,2868,1630,1566,1538,1503 /cm.
$[\alpha]_D$=+38.8° (MeOH,c=1.01,22°C).

No.2a.97

[0205] CD_3OD 300MHz
0.93(1H,d,J=9.9Hz),1.13 and 1.22(each 3H,each s),1.48-1.58(3H,m),1.96-2. 36(11H,m),4.10(1H,m),5.35-5.50(2H,m), 7.42-7.51(2H,m),8.06(1H,m).
IR(KBr):3447,3087,2987,2922,2868,1629,1545,1501 /cm.
$[\alpha]_D$=+52.9° (MeOH,c=1.01,24°C).

No.2a.98

[0206] $[\alpha]_D$=+53.2° (MeOH,c=1.02,23°C).

No.2a-99

[0207] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.12 and 1.22(each 3H,each s),1.26.2.45(24H,m),4.2 5(2H,m),5.34-5.52(2H,m),6.18(1H,d, J=8.7Hz),6.91 and 7.66(each 2H,each d,J=9.0Hz).
IR($CHCl_3$):3455,3029,3019,2939,2862,1738,1709,1645,1605,1523,1494 /cm.
$[\alpha]_D$=+51.4° (MeOH,c=1.00,23°C).

No.2a-100

[0208] $[\alpha]_D$=+49.3° (MeOH,c=1.00,24°C).

No.2a-101

[0209] $[\alpha]_D$=+51.3° (MeOH,c=1.00,24°C).

No.2a-102

[0210] $[\alpha]_D$=+48.8° (MeOH,c=1.01,23°C).

No.2a-103

[0211] $CDCl_3$ 300MHz
0.94(1H,d,J=10.2Hz),1.12 and 1.22(each 3H,each s),1.52-2.46(14H,m),2.4 8(3H,d,J=0.3Hz),4.20(1H,m),5.32-5.54(2H, m),6.46(1H,brs),7.12(1H,d,J=9.0 Hz).
IR($CHCl_3$):3415,3144,3029,3011,2926,2871,1708,1671,1598,1538,14564 /cm
$[\alpha]_D$=+49.6° (MeOH,c=1.01,23°C).

No.2a-104

[0212] $[\alpha]_D$=+77.0° (MeOH,c=1.02,23°C).

No.2a-105

[0213] $CDCl_3$ 300MHz
93(1H,d,J=9.9Hz),1.09 and 1.21(each 3H,each s),1.51-2.44(14H,m),3.90(6 H,s),4.20(1H,m),5.38-5.50(2H,m),5.87(1H, d,J=9.0Hz),6.25 and 7:54 (each 1H,each d,J=15.6Hz),6.84(1H,d,J=8.1Hz),7.03(1H,d,J=1.8Hz),7.09(1 H,dd,J=1.8 and 8.1Hz).
IR($CHCl_3$):3439,3028,3012,2937,2871,2841,1739,1708,1661,1620,1600,1513 /cm.
$[\alpha]_D$=+77.3° (MeOH,c=1.01,23°C).

No.2a-106

[0214] $[\alpha]_D$=+67.0° (MeOH,c=1.00,25°C)

No.2a.107

[0215] $[\alpha]_D$=+66.6° (MeOH,c=1.01.24°C).
m.p.168.0-170.0°C

No.2a-108

[0216] $[\alpha]_D$=+61.8° (MeOH,c=1.00,22°C).

No.2a-109

[0217] $CDCl_3$ 300MHz
0.96(1H,d,J=10.2Hz),1.10 and 1.22(each 3H,each s),1.51-2.45(14H,m).4.2 5(1H,m),5.33-5.49(2H,m),6.21(1H,d, J=8.7Hz),7.25 and 7.60(each 2H,each d,J=8.7Hz),7.33-7.41(5H,s).
IR($CHCl_3$):3453,3062,3028,3014,2925,2870,1739,1708,1651,1594,1557,1515, 1481 /cm.
$[\alpha]_D$=+61.0° (MeOH,c=1.01,22°C).

No.2a-110

[0218] CD_3OD 300MHz
0.94(1H, d, J=9.9Hz),1.13 and 1.22(each 3H,each s), 1.54.2.37(14H, m), 4.12(1H, m), 5.38-5.49(2H, m),7.25 and 7.68

(each 2H,each d, J=8.7Hz), 7.41(5H,s)
IR(KBr):3435,3058,2986,2920,2866,1635,1595,1562,1521,1482,1439,1411 /c m.
$[\alpha]_D$=+47.3° (MeOH, c=1.01,23°C).

No.2a-111

[0219] $[\alpha]_D$=+65.6° (MeOH,c=1.01,24°C).

No.2a-112

[0220] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.12 and 1.23(each 3H,each s),1.51-2.46(14H,m),4.2 7(1H.m),5.35-5.50(2H,m),6.22(1H,d, J=8.4Hz),7.40 and 7.66(each 2H,each d,J=9.0 H z) .
IR($CHCl_3$):3439,3028,3012,2937,2871,2841,1739,1708,1661,1620,1600,1513 /cm.
$[\alpha]_D$=+65.6° (MeOH,c=1.01,22°C)

No.2a-113

[0221] $[\alpha]_D$=59.6° (MeOH,c=1.00,24°C).

No.2a-114

[0222] $CDCl_3$ 300MHz
0.98(1H,d,J=10.2Hz),1.12 and 1.24(each 3H,each s),1.52-2.46(14H,m),4.2 9(1H,m),5.35-5.51(2H,m),6.28(1H,d, J=8.4Hz),7.70 and 7.83(each 2H,each d,J=8.4Hz).
IR($CHCl_3$):3439,3028,3012,2937,2871,2841,1739,1708,1661,1620,1600,1513 /cm.
$[\alpha]_D$=+60.6° (MeOH,c=1.01,22°C).

No.2a-115

[0223] $[\alpha]_D$=+59.7° (MeOH,c=0.99,24°C).

No.2a-116

[0224] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.12 and 1.23(each 3H,each s),1.52-2.46(14H,m),2.3 9(3H,s),4.27(1H,m),5.33-5.51(2H,m),6.24 (1H,d,J=9.0Hz),7.23 and 7.62 (each 2H,each d,J=8.4Hz).
IR($CHCl_3$):3439,3028,3012,2937,2871,2841,1739,1708,1661,1620,1600,15131 cm.
$[\alpha]_D$=+59.7° (MeOH,c=0.99,24°C).

No.2a-117

[0225] $[\alpha]_D$=+56.7° (MeOH,c= 1.00,23°C).

No.2a-118

[0226] $CDCl_3$ 300MHz
0.96(1H,d,J=10.2Hz),1.11 and 1.23(each 3H,each s),1.53-2.44(14H,m),4.2 3(1H,m),5.34-5.51(2H,m),6.02(2H,s),6.13 (1H,d,J=8.7Hz),6.83(1H,dd,J=1.2 and 7.8Hz),7.22.7.25(2H,m).
IR($CHCl_3$):3453,3031,3020,3012,2924,2870,1740,1708,1650,1619,1605,1519, 1504,1480 /cm.
$[\alpha]_D$=+57.2° (MeOH,c=1.02,23°C).

No.2a-119

[0227] $CDCl_3$ 300MHz
0.96(1H,d,J=10.5Hz),1.07 and 1.23(each 3H,each s),1.51-2.44(14H,m),2.3 2(3H,s),4.26(1H,m),5.37-5.52(2H,m),6.40 (1H,d,J=9.0Hz),7.09(1H,m),7.30(1 H,m),7.46(1H,m),7.66(1H,m).
IR($CHCl_3$):3443,3028,3012,2925,2870,1766,1747,1709,1657,1607,1516,1479 /cm.

$[\alpha]_D$=+53.2° (MeOH,c=0.99,21°C).

No.2a-120

[0228] $CDCl_3$ 300MHz
0.98(1H,d,J=10.2Hz),1.14 and 1.24(each 3H,each s), 1.53-2.44(14H,m),4.3 0(1H,m), 5.35-5.52(2H,m), 6.42(1H,d, J=8.7Hz), 6.85(1H,m), 6.99(1H,dd,J=1.2 and 8.4Hz), 7.27(1H,m), 7.39(1H,m).
IR($CHCl_3$):3463,3033,3021,3014,2992,2924,2870,1708,1643,1597,1523,1488 /cm.
$[\alpha]_D$=+46.3° (MeOH,c=1.01,21°C).

No.2a-121

[0229] $CDCl_3$ 300MHz
0.98(1H,d,J=10.2Hz),1.14 and 1.23(each 3H, each s),1.47.2.47(14H,m),3.9 5(3H,s),4.31(1H,m),5.32-5.50(2H,m),6.98 (1H,dd,J=0.9 and 8.4Hz).7.09(1H. ddd,J=0.9,7.7 and 8.4Hz),7.45(1H,m),8.19(1H,dd,J=2.1 and 8.1Hz),8.32(1 H, d, J=9.0Hz).
IR($CHCl_3$):3400,3078,3028,3020,3007,2924,2870,2842,1736,1708,1640,1600, 1536,1483,1470 /cm.
$[\alpha]_D$=+38.1° (MeOH,c=1.02,23°C).

No.2a-122

[0230] $[\alpha]_D$=+42.3° (MeOH,c=0.99,23°C).

No.2a-123

[0231] $[\alpha]_D$=+38.7° (MeOH,c=1.00,21°C).

No.2a-124

[0232] $[\alpha]_D$=+45.0° (MeOH,c=1.01,21°C).
m.p.119.0-120.0°C

No.2a-125

[0233] $[\alpha]_D$=+49.8° (MeOH,c=1.01,22°C).

No.2a-126

[0234] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.11 and 1.23(cach 3H,each s),1.52-2.47(14H,m),4.2 6(1H,m),5.34-5.50(2H,m),6.22(1H,d, J=8.7Hz),7.55-7.61(4H,m).
IR($CHCl_3$):3400,3078,3028,3020,3007,2924,2870,2842,1736,1708,1640,1600, 1536,1483,1470 /cm.
$[\alpha]_D$=+63.0° (MeOH,c=1.01,23°C).

No.2a-127

[0235] $CDCl_3$ 300MHz
0.91(1H,d.J=10.2Hz),1.10 and 1.20(each 3H,each s),1.50-2.42(14H,m),4.2 3(1H,m),5.31-5.51(2H,m),6.45(1H,d, J=8.4Hz),7.01(1H,t,J=7.4Hz),7.22-7.27(2H,m),7.33-7.40(4H,m),7.53(2H,d,J=9.0.Hz),8.30 and 8.48(each 1H, each s)
IR($CHCl_3$):3452,3028,3022,3015,2925,2870,1708,1654,1590,1514,1478 /cm.
$[\alpha]_D$=+59.5° (MeOH,c=1.01,23°C).

No.2a-128

[0236] d_6-DMSO 300MHz
0.84(1H,d,J=9.9Hz),1.06 and 1.19(each 3H,each s),1.37-2.37(14H,m),3.79(1H,m),5.35-5.51 (2H,m),6.08(1 H, d, J=8.7Hz),6.85-6.90(1H,m), 7.18-7.23(2H, m),7.35-7.38(2H,m),8.42(1H,s),12.00(1H,s).
IR(Nujol):3395,3345,2925,2866,2623,2506,1697,1658,1638,1597,1557 /cm.

$[\alpha]_D$=+26.0° (MeOH,c=1.01,23°C).
m.p. 164.0-166.0°C

No.2a-129

[0237] $CDCl_3$ 300MHz
1.01(1H,d,J=10.0Hz),1.17 and 1.25(each 3H,each s),1.54-2.52(14H,m),4.3 4(1H,m),5.36-5.57(2H.m),6.42(1H,d, J=8.6Hz),7.51-7.60(2H,m),7.77(1H,dd,J =1.8 and 8.6Hz),7.85-7.96(3H,m),8.24(1H,brs).
IR($CHCl_3$):3451,3060.3028,3010,2925,2870,1708,1652,1629,1600,1517,1502 /cm.
$[\alpha]_D$=+68.6° (MeOH,c=1.00,22°C).

No.2a-130

[0238] $CDCl_3$ 300MHz
1.02(1H,d,J=10.2Hz),1.04 and 1.26(each 3H,each s), 1.54-2.52(14H,m),4.4 1(1H,m),5.41-5.58(2H,m),6.14(1H,d, J=9.0Hz),7.43-7.59(4H,m),7.85-7.92(2H, m),8.27(1H,dd,J=1.8 and 7.2Hz).
IR($CHCl_3$):3436,3032,3010,2924,2870,2664,1708,1652,1512,1498 /cm.
$[\alpha]_D$=+93.9° (MeOH,c=1.00,22°C)
m.p.94.0-96.0°C

No.2a-131

[0239] $[\alpha]_D$=+50.2° (MeOH,c=0.95,21°C).

No.2a-132

[0240] $[\alpha]_D$=+10.9° (MeOH,c=0.92,21°C).

No.2a-133

[0241] $[\alpha]_D$=+60.4° (MeOH,c=1.00,21°C).

No.2a-134

[0242] $[\alpha]_D$=+38.5° (MeOH,c=1.01,23°C).

No.2a-135

[0243] $[\alpha]_D$=+52.5° (MeOH,c=1.01,23°C).
m.p.180.0-182.0°C

No.2a-136

[0244] $[\alpha]_D$=+35.3° (MeOH,c=1.02,23°C).
m.p.79.0-80.0°C

No.2a-137

[0245] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.11 and 1.22(each 3H,each s),1.43(3H;t.J=6.9Hz),1. 52-2.44(14H,m),4.03(2H,q,J=6.9Hz),4.26 (1H,m),5.33-5.50(2H;m),6.19(1H,d, J=8.7Hz),6.88-7.00(6H,m),7.65-7.68(2H,m).
IR($CHCl_3$):3455,3031,3024,3014,2988,2925,2870,1741,1708,1649,1602,1521, 1504,1490 /cm.
$[\alpha]_D$=+52.0° (MeOH,c=1.01,23°C).

No.2a-138

[0246] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.11 and 1.22(each 3H,each s),1.35(6H,d,J=6.0Hz),1. 53-2.46(14H,m),4.25(1H,m),4.51(1H,m),

5.33-5.50(2H,m),6.12(1H,d,J=9.0Hz),6.87-6.99(6H,m),7.65-7.68(2H,m).
IR($CHCl_3$):3454,3031,3014,2980,2925,2870,1741,1708,1649,1602,1522,1490 /cm.
$[\alpha]_D$=+500° (MeOH,c=1.05,22°C).

No.2a-139

[0247] $CDCl_3$ 300MHz
1.00(1H,d,J=10.2Hz),1.16 and 1.24(each 3H,each s),1.59-2.52(14H,m),4.3 1(1H,m),5.40-5.53(2H,m),6.36(1H,d, J=8.7Hz),6.70(1H,d,J=1.5Hz),7.12(1H, m),7.30(1H,m),7.47(1H,dd,J=0.6 and 8.1Hz),7.61(1H,d,J=8.4Hz).
IR($CHCl_3$):3449,3243,3029,3022,3013,2925,2871,1707,1631,1542,1505 /cm. $[\alpha]_D$=+63.4° (MeOH,c=1.00,23°C).
m.p.178.0-179.0°C

No.2a-140

[0248] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.18 and 1.23(each 3H,each s),1.57-2.50(14H,m),4.3 5(1H,m),5.32-5.55(2H,m),6.42(1H,d, J=8.7Hz),6.70(1H,d;J=1.5Hz),7.21-7.24(2H m),7.46(1H,m),7.76(1H,m),7.86(1H,d,J=3.0Hz),10.20(1H,s)
IR($CHCl_3$):3465,3010,2924,1739,1604,1546,1504 /cm.
$[\alpha]_D$=+39.4° (MeOH,c=1.01.22°C).
m.p.167.0-168.0°C

No.2a-141

[0249] $CDCl_3$ 300MHz
0.99(1H,d,J=10.2Hz),1.14 and 1.24(each 3H,each s),1.55-2.44(14H,m),3.8 4(3H,s),4.27(1H,m),5.34-5.52(2H,m),6.28 (1H,d,J=9.0Hz),6.91 and 7.47 (each 2H,each d,J=9.0Hz),6.98 and 7.14(each 1H, each d,J=16.5Hz),7.54 and 7.70(each 2H,eachd,J=8.7Hz).
IR($CHCl_3$):3453,3025,3015,2925,2870,2839,1740,1708,1649,1602,1510,1493, 1470 /cm.
$[\alpha]_D$=+73.4° (MeOH,c=1.02,22°C).
m.p.155.0-157.0°C

No.2a-142

[0250] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.11 and 1.23(each 3H,each s),1.52-2.45(14H,m),3.7 9(3H,s),4.27(1H,m),5.34-5.50(2H,m),6.24 (1H,d,J=9.0Hz),6.49 and 6.62 (each 1H each d,J=12.3Hz),6.77 and 7.16(each 2H, each d,J=8.7Hz),7.32 and 7.59(each 2H, each d,J=8.1Hz).
IR($CHCl_3$):3453,3025,3014,2925,2870,2839,1739,1708,1649,1606,1510, 1494 /cm.
$[\alpha]_D$=+60.7° (MeOH,c=0.99,22°C).

No.2a-143

[0251] $[\alpha]_D$=+57.3° (MeOH,c=1.01,23°C).

No.2a-144

[0252] $[\alpha]_D$=+12.2° (MeOH,c=1.00,23°C).
m.p.114.0-116.0°C

No.2a-145

[0253] $CDCl_3$ 300MHz
0.95(1H,d,J=10.2Hz),1.10 and 1.21(each 3H,each s),1.52-2.44(14H,m),4.2 5(1H,m),5.33-5.49(2H,m),6.37(1H,d, J=8.7Hz),7.45-7.47(3H,m),7.62-7.66(2H, m),7.69 and 7.80(each 2H,each d, J=7.5Hz,).
IR($CHCl_3$):3449,3058,3027,3012,2925,2870,1708,1655,1513,1481,1043 /cm.
$[\alpha]_D$=+61.0° (MeOH,c=1.01,23°C).

No.2a-146

[0254] $CDCl_3$ 300MHz
0.95(1H,d,J=10.5Hz),1.09 and 1.21(each 3H,each s),1.50-2.41(14H,m),4.2 5(1H,m),5.33.5.49(2H,m).6.33(1H,d, J=8.4Hz),7.49-7.61(3H,m),7.91-7.92(2H, m),7.82 and 7.97(each 2H,each d,J=8.7Hz,).
IR($CHCl_3$):3447,3029,3023,3015,2925,2870,1708,1660,1514,1484,1321,1161 /cm.
$[\alpha]_D$=+62.0° (MeOH,c=1.00,22°C).

No.2a-147

[0255] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.12 and 1.23(each 3H,each s),1.52-2.46(14H,m),2.5 1(3H,s),4.26(1H,m),5.34-5.51(2H,m),6.23 (1H,d,J=8.4Hz),7.26 and 7.64 (each 2H,each d,J=8.4Hz).
IR($CHCl_3$):3453.3027,3015,2925,2870,2665,1708,1648,1596,1516,1484 /cm.
$[\alpha]_D$=+67.7° (MeOH,c=0.82,22°C).

No.2a-148

[0256] $[\alpha]_D$=+72.5° (MeOH,c=1.01,25°C).

No.2a-149

[0257] $[\alpha]_D$=+67.8° (MeOH,c=0.98,25°C).

No.2a-150

[0258] $CDCl_3$ 300MHz
0.94(1H,d,J=10.2Hz),1.10 and 1.23(each 3H,each s),1.52-2.50(14H,m),4.2 2(1H,m),5.36-5.55(2H,m),6.48(1H,d, J=8.4Hz),8.35(1H,s),8.90(1H,s).
IR($CHCl_3$):3443,3374,3091,3024,3012,2925,2871,1709,1652,1525,1494 /cm. $[\alpha]_D$=+58.1° (MeOH,c=1.01,23°C).
m.p.120.0-122.0°C

No.2a-151

[0259] $[\alpha]_D$=+40.6° (MeOH,c=1.01,23°C).

No.2a-152

[0260] $CDCl_3$ 300MHz
0.96(1H,d,J=10.5Hz),1.10 and 1.24(each 3H, each s),1.50-2.50(l4H,m),2.7 1(3H,s),4.26(1H,m),5.37-5.51(2H,m),6.02 (1H,d,J=9.OHz),8.73(1H,s).
IR($CHCl_3$):3463,3435.3087.3025.3014,2925,2870.1708.1649,1523.1503 /cm. $[\alpha]_D$=+54.1 ° (MeOH,c=1.02,22°C).

No.2a-153

[0261] $CDCl_3$ 300MHz
0.95(1H,d,J=9.9Hz),1.11 and 1.23(each 3H,each s),1.50.2.50(14H,m),2.50(3H,s),4.26(1H,m),5.36-5.51(2H,m),6.01 (1H,d,J=8.4Hz),6.88(1H,d,J=5.1Hz), 7.26(1H,d,J=5.1Hz).
IR($CHCl_3$):3469,3431,3025,3013,2925,2871,2664,1708,1639,1544,1505 /cm.
$[\alpha]_D$=+35.8° (MeOH,c=1.03,22°C).

No.2a-154

[0262] $CDCl_3$ 300MHz
0.95(1H,d,J=9.9Hz),1.10 and 1.22(each 3H,each s),1.52.2.46(14H,m),2.51(3H,d,J=1.2Hz),4.26(1H,m),5.34-5.50(2H, m),6.00(1H,d,J=8.4Hz),6.73(1H,dd, J=5.1 and 3.6Hz),7.29(1H,d,J=3.6Hz).
IR($CHCl_3$):3450,3431,3026,3011,2925,2869,1739,1708,1639,1547,1508 /cm.
$[\alpha]_D$=+50.5° (MeOH,c=1.01,22°C).

No.2a-155

[0263] $CDCl_3$ 300MHz
0.99(1H,d,J=10.2Hz),1.19 and 1.25(each 3H,each s),1.53-2.48(14H,m),4.3 1(1H,m),5.36-5.51(2H,m),6.79(1H,d, J=9.3Hz),7.29(1H,m),7.41(1H,m),7.48(1 H,s),7.51(1H,m),7.66(1H,d,J=8.1Hz).
IR($CHCl_3$):3436, 3029, 3024, 3015, 2925, 2871, 2670, 1708, 1659, 1598, 1510 /cm.
$[\alpha]_D$=+69.1° (MeOH,c=1.01,22°C).

No.2a.156

[0264] $CDCl_3$:CD_3O_D=10:1 300MHz
0.99(1H,d,J=9.9Hz),1.11 and 1.21(each 3H,each s),1.56-2.58(14H,m),4.22(1H,m),5.35-5.59(2H,m),6.83(1H.d, 1=8.4Hz),7.48(1H,d.J=8:4Hz),7.61(1H,dd, J=1.5 and 8.4Hz),8.09(1H,d,J=1.5Hz),8.12(1H,s).
IR(KBr):3422,3115,2985,2922,2869,2609,1708,1636,1578,1529,1470 /cm.
$[\alpha]_D$=+62.8° (MeOH,c=1.01,22°C).

No.2a-157

[0265] $[\alpha]_D$=+40.0° (MeOH,c=0.95,22°C).

No.2a-158

[0266] $CDCl_3$ 300MHz
1.00(1H,d,J=10.5Hz),1.17 and 1.24(each 3H,each s),1.54-2.50(14H,m),4.3 4(1H,m),5.36-5.52(2H,m),7.80(1H,d, J=9.0Hz),9.30(1H,s).
IR($CHCl_3$):3410,3122,3030,3012,2925,2871,2668,1709,1667,1538,1466 /cm.
$[\alpha]_D$=+44.9° (MeOH,c=0.99,22°C).

No.2a-159

[0267] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.13 and 1.22(each 3H,each s),1.55-2.43(l4H,m),3.0 3(6H,s),4.23(1H,m),5.32-5.51(2H,m),6.16 (1H,d,J=8.7Hz),6.87 and 7.63 (each 2H,each d,J=8.7Hz).
IR($CHCl_3$):3457,3028,3006,2924,2870,2654,1739,1709,1637,1608,1608,1534, 1501 /cm.
$[\alpha]_D$=+64.8° (MeOH,c=1.01,22°C).

No.2a-160

[0268] d_6-DMSO 300MHz
0.83(1H,d,J=9.9Hz).1.02 and 1.19(each 3H,each s),1.38-1.61(3H,m),1.90-2. 32(11H,m),3.90(1H,m),5.41.5.44(2H,m), 7.32(1H,dd,J=0.9 and 7.2Hz),7.45. 7.60(2H,m),7.77(1H,dd,J=0.9 and 7.8Hz),8.03(1H,d,J=6.9Hz),12.40(1H,s).
IR(Nujol):3315,2924,2856,2656,2535,1737,1703,1637,1598,1581,1541 /cm.
$[\alpha]_D$=+78.5° (MeOH,c=1.01,24°C).
m.p.161.0-162.0°C

No.2a-161

[0269] $[\alpha]_D$=+65.3° (MeOH,c=1.00.22°C).

No.2a-162

[0270] $CDCl_3$ 300MHz
0.99(1H,d,J=10.2Hz),1.13 and 1.25(each 3H,each s),1.53-2.45(14H,m),4.3 0(1H,m),5.36-5.51(2H,m),6.32(1H,d, J=8.4Hz),7.88 and 8.28(each 2H,each d, J=9.0Hz) .
IR($CHCl_3$):3448,3029,3016,2925,2870,1708,1664,1602,1527,1484,1347 /cm.
$[\alpha]_D$=+72.7° (MeOH,c=1.02,22°C).
[0271] No.2a-163
[0272] $CDCl_3$ 300MHz.

0.96(1H,d,J=10.2Hz),1.11 and 1.23(each 3H,each s),1.55-2.51(14H,m),4.2 6(1H,m),5.36-5.57(2H,m),6.68(1H,d, J=7.8Hz),7.41(1H,dd,J=4.8 and 8.1Hz), 8.20(1H,d,J=8.1Hz),8.66(1H,d,J=4.8Hz),9.00(1H,s).
IR($CHCl_3$):3448,3026,3013,2925,2870,2534,1709,1658,1590,1515,1471 /cm.
$[\alpha]_D$=+71.3° (MeOH,c=1.01,22°C).

No.2a-164

[0273] $[\alpha]_D$=+40.8° (MeOH,c=0.98,22°C).

[0274] No.2a-165

$CDCl_3$ 300MHz
0.96(1H,d,J=10.5Hz),1.11 and 1.24(each 3H, each s),1.55-2.52(14H,m), 4.2 4(1H,m),5.37-5.57(2H,m),6.63(1H, d.J=7.8Hz),7.59 and 8.63(each 2H each d,J=6.0Hz).
IR($CHCl_3$):3447,3346,3028,3016,2925,2870,2538,1941,1708,1662,1556,1516 /cm.
$[\alpha]_D$=+75.4° (MeOH,c=1.01,22°C).

[0275] No.2a-166

$CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.11 and 1.22(each 3H,each s),1.51-2:44(14H,m),2.9 5(6H,s),4.25(1H,m),5.33-5.50(2H,m),6.19 (1H,d,J=8.7Hz),6.77 and 6.97 (each 2H, each d,J=8.4Hz),6.94 and 7.65(each 2H,each d,J=9.0Hz).
IR($CHCl_3$):3453,3024,3016,2924,2871,2806,1739,1708,1647,1612,1604,1515, 1490 /cm.
$[\alpha]_D$=+53.1° (MeOH,c=1.02,23°C).
m.p.104.0-105.5°C

No.2a-167

[0276] $CDCl_3$ 300MHz
1.01(1H,d,J=9.9Hz),1.19 and 1.26(each 3H,each s),1.56-2.53(14H,m),4.37(1H,m),5.35-5.55(2H,m),6.47(1H,d, J=8.4Hz),7.61-7.71(2H,m),7.79(2H,s),7.89 -7.97(2H,m),8.27(1H,d,J=2. 1Hz),8.66-8.73(2H,m).
IR($CHCl_3$):3450,3024,3014,2925,2870,2667,1707,1650,1531,1509 /cm.
$[\alpha]_D$=+70.5°(MeOH,c=1.00,22°C).

No.2a-168

[0277] $CDCl_3$ 300MHz
1.02(1H,d,J=10.2Hz), 1.20 and 1.26(each 3H,each s),1.56-2.50(14H,m),4.3 8(1H,m), 5.36-5.56(2H,m), 6.51(1H,d, J=8.9Hz), 7.61-7.93(7H,m), 8.74(1H,d,J= 8.4Hz), 9.15(1H,s).
IR($CHCl_3$):3517,3451,3060,3028,3011,2925,2870,2664,1709,1651,1519,1498/cm.
$[\alpha]_D$=+54.4° (MeOH,c=1.00,23°C).

No.2a-169

[0278] $CDCl_3$ 300MHz
0.96(1H,d,J=10.5Hz),1.09 and 1.21(each 3H,each s),1.50-2.44(14H,m),3.8 5(3H,s),4.24(1H,m),5.32-5.48(2H,m),6.19 (1H,d,J=8.4Hz),6.94 and 7.45 (each 2H,each d,J=9.0Hz),7.11 and 7.45(each 2H,each d,J=8.7Hz).
IR($CHCl_3$):3516,3453,3029,3009,2925,2870,2840,2665,1708,1650,1593,1515, 1493,1482 /cm.
$[\alpha]_D$=+57.8° (MeOH,c=1.00,23°C).

No.2a-170

[0279] $CDCl_3$ 300MHz
0.98(1H,d,J=10.2Hz), 1.15 and 1.24(each 3H,each s), 1.52-2.50(14H,m),4.2 8(1H,m), 5.33-5.54(2H,m), 6.25(1H,d, J=8.2Hz), 7.38-7.44(2H,m), 7.74(1H,s), 7. 81-7.86(2H,m).
IR($CHCl_3$):3517,3448,3427,3024,3013,2925,2870,2669,1708,1650,1562,1535, 1500 /cm.
$[\alpha]_D$=+61.6° (MeOH,c=1.00,23°C).

No.2a-171

[0280] $CDCl_3$ 300MHz
0.96(1H,d,J=10.2Hz, 1.11 and 1.22(each 3H,each s), 1.52-2.42(14H,m), 2.48 (3H,s), 4.21(1H,m), 5.31-5.52(2H,m), 6.06

(1H,d,J=8.2Hz), 6.97 and 7.59 (e ach 1H,each d,J=1.2Hz).
IR($CHCl_3$):3452,3113,3028,3007,2925,2870,2669,1708,1645,1554,1509 /cm.
$[\alpha]_D$=+52.4° (MeOH,c=1.00,23°C).

No.2a-172

[0281] $CDCl_3$ 300MHz
0.96(1H,d,J=10.2Hz),1.09 and 1.28(each 3H,each s),1.50-2.40(14H,m),2.6 9(3H,s),4.24(1H,m),5.35-5.51(2H,m),5.96 (1H,d,J=8.7Hz),7.03 and 7.07 (each 1H,each d,J=5.4Hz).
IR($CHCl_3$):3451,3031,3013,2925,2870,2666,1708,1647,1542,1497 /cm.
$[\alpha]_D$=+51.2° (MeOH,c=1.00,23°C).

No.2a-173

[0282] $CDCl_3$ 300MHz
0.95(1H,d,J=10.2Hz),1.10 and 1.23(each 3H,each s),1.50-2.45(14H,m),4.2 2(1H,m),5.35-5.49(2H,m),6.05(1H,d, J=8.4Hz),7.26 and 7.75(each 1H,each d,J=1.5Hz).
IR($CHCl_3$):3451,3011,3029,3011,2925,2870,1708,1652,1538,1500 /cm.
$[\alpha]_D$=+50.6° (MeOH,c=1.01,23°C).

No.2a-174

[0283] $CDCl_3$ 300MHz
0.96(1H,d,J=10.2Hz),1.13 and 1.23(each 3H,each s),1.52-2.50(14H,m),4.2 9(1H,m),5.35-5.51(2H,m),7.02(1H,d, J=8.4Hz),7.32 and 8.16(each 1H,each d,J=3.9Hz).
IR($CHCl_3$):3417,3115,3023,3014,2925,2870,1708,1645,1530 /cm.
$[\alpha]_D$=+48.8° (MeOH,c=1.02,23°C).

No.2a-175

[0284] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.14 and 1.23(each 3H,each s),1.50-2.52(14H,m),2.5 2(3H,s),4.29(1H,m),5.34-5.51(2H,m),7.78 (1H,d,J=9.0Hz),7.24 and 7.52 (each 1H,each d,J=5.4Hz).
IR($CHCl_3$):3329,3093,3023,3015,2924,2871,1708,1640,1526 /cm. $[\alpha]_D$=+45.0° (MeOH,c=1.01,23°C).

No.2a-176

[0285] $CDCl_3$ 300MHz
0.95(1H,d,J=10.5Hz),1.09 and 1.23(each 3H,each s),1.52-2.46(14H,m),2.4 0(3H,d,J=0.9Hz),4.24(1H,m),5.35-5.51(2H, m),6.05(1H,d,J=8:7Hz),6.95(1H, m),7.57(1H,d,J=3.3Hz).
IR($CHCl_3$):3517,3444,3103,3024,3013.2926,2870,1739,1748,1649,1636,15071 cm.
$[\alpha]_D$=+54.8° (MeOH,c=1.01,23°C).
m.p.97.0-99.0°C

No.2a-177

[0286] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz), 1.11 and 1.23(each 3H,each s), 1.52-2.45(14H,m), 3.9 3(3H,s), 4.27(1H,m), 5.34-5.50(2H,m), 6,35(1H,d,J=3.3Hz), 7.80(1H,d,J=8.7Hz), 8.10(1H,d,J=3.3Hz).
IR($CHCl_3$):3395,3121,3031,3019,3012,2925,2871,1739,1709,1640,1557,1533 /cm.
$[\alpha]_D$=+22.8° (MeOH,c=1.01,23°C).
m.p.109.0.112.0°C

No.2a-178

[0287] $CDCl_3$ 300MHz
0.96(1H,d,J=10.5Hz),1.10 and 1.23(each 3H,each s), 1.51-2.45(14H, m),4.2 4(1H,m),5.35-5.50(2H,m),6.09(1H,d, J=8.4Hz),7.17-7.31(6H,m),7.95(1H,d,J= 1.5Hz).

IR($CHCl_3$):3510,3451,3062,3031,3022,3011,2925,2870,2662,1708,1651,1582, 1535,1497,1477/cm.
$[\alpha]_D$=+47.9° (MeOH,c=1.01,25°C).

No.2a-179

[0288] $CDCl_3$ 300MHz
0.96(1H,d,J=10.2Hz),1.14 and 1.24(each 3H,each s),1.52-2.48(14H,m),4.3 0(1H,m),5.36-5.52(2H,m),6.73(1H,d, J=9.0Hz),6.26 and 7.37(each 1H,each d.J=6.0Hz).
IR($CHCl_3$):3509,3429,3115,3094,3025,3014,2925,2871,2666,1708,1649,1529, 1510 /cm.
$[\alpha]_D$=+51.0° (MeOH,c=1.02,25°C).

No.2a-180

[0289] $CDCl_3$ 300MHz
0.95(1H,d,J=10.2Hz),1.14 and 1.24(each 3H,each s),1.52.2.46(14H,m),3.8 9(3H,s),4.21(1H,m),5.35-5.50(2H,m),6.05 (1H,d,J=8.4Hz),6.46 and 7.04 (each 1H,each d,J=1.8Hz).
IR($CHCl_3$):3516,3450,3114.3031,3010.2925.2871,1708,1648,1546,1511,1477 /cm.
$[\alpha]_D$=+49.1° (MeOH,c=1.01,25°C).

No.2a-181

[0290] $CDCl_3$ 300MHz
0.97(1H.d.J=10.2Hz).1.14 and 1.23(each 3H,each s),1.52-2.48(14H,m),2.4 2(3H,s),4.31(1H,m),5.34-5.52(2H,m),8.07 (1H,d,J=9.3Hz),7.27 and 8.17 (each.1H,each d,J=3.3Hz).
IR($CHCl_3$):3510,3301,3112,3023,3007,2924,2871,2663,1708,1636,1534 /cm.
$[\alpha]_D$=+41.0° (MeOH,c=0.96,25°C).

No.2a-182

[0291] $CDCl_3$ 300MHz
0.96(1H,d,J=10.2Hz),1.11 and 1.23(each 3H,each s),1.53-2.46(14H,m),2.5 1(3H,s),4.21(1H,m),5.35-5.51(2H,m),6.05 (1H,d,J=8.1Hz),7.26 and 7.78 (each 1H,each d,J=1.8Hz).
IR($CHCl_3$):3509,3450,3109,3024,3012,2925,2870,2666,1708,1650,1535,1 498,1471 /cm.
$[\alpha]_D$=+52.9° (MeOH,c=0.95,25°C).

No.2a-183

[0292] $CDCl_3$ 300MHz
0.96(1H,d,J=10.5Hz),1.12 and 1.22(each 3H,each s),1.52-2.46(14H,m),4.2 5(1H,m),5.33-5.51(2H,m),6.17(lH,d, J=8.7Hz),7.01-7.05(3H,m).7.l4 and 7.6 2(each 2H,each d,J=8.7Hz),7.27-7.34(2H,m).
IR($CHCl_3$):3428,3026,3015,2925,2870,2666,1739,1708,1643,1613,1594,1526, 1499 /cm.
$[\alpha]_D$=+64.8° (MeOH,c=1.02,23°C).

No.2a-184

[0293] $CDCl_3$ 300MHz
1.01(1H,d,J=10.2Hz),1.18 and 1.26(each 3H,each s), 1.55-2.50(14H,m),4.3 5(1H,m),5.35-5.55(2H,m),6.42(1H,d, J=8.7Hz),7.46-7.52(2H, m).7.73(1H, dd,J =1.8 and 8.4Hz),7.83-7.89(2H,m),8.21(1H,m),8.59(1H,d,J=1.5Hz).
IR($CHCl_3$):3451,3031,3014,2925,2870,2660,1739,1708,1650,1604,1513,1463 /cm.
$[\alpha]_D$=+58.3° (MeOH,c=1.00,23°C).

No.2a-185

[0294] $CDCl_3$ 300MHz
1.00(1H,d,J=10.2Hz),1.18 and 1.25(each 3H,each s),1.55-2.50(14H,m),4.3 4(1H,m),5.35-5.54(2H,m),6.36(1H,d, J=8.7Hz),7.37(1H,t,J=7.4Hz),7.50(1H,m),7.57-7.59(2H,m),7.79(1H,dd,J=1.8 and 8.1Hz),7.99(1H,d,J=7.8Hz),8.39(1 H,d,J=1.8Hz).
IR($CHCl_3$):3451,3030,3020.2870,2665.1708.1652.1632,1603,1586,1514,1469, 1448 /cm.

$[\alpha]_D$=+59.4° (MeOH,c=1.01,24°C).

No.2a-186

[0295] $CDCl_3$ 300MHz
1.00(1H,d.J=10.5Hz),1.17 and 1.25(each 3H,each s),1.54-9.50(14H,m),4.3 3(1H,m),5.35-5.54(2H,m),6.37(1H,d, J=8.7Hz),7.37(1H,t,J=7.4Hz),7.51(1H,t, J=7.8Hz),7.56(1H,m).7.70(1H.dd,J=1.2 and 8.4Hz),7.97(3H,m).
IR($CHCl_3$):3451,3030,3014,2924,2870,2671,1739,1708,1652,1577,1517,1488, 1471 /cm.
$[\alpha]_D$=+72.2° (MeOH,c=1.00,24°C).

No.2a-187

[0296] $CDCl_3$ 300MHz
1.00(1H,d,J=9.8Hz),1.18 and 1.25(each 3H,each s),1.54-2.53(14H,m),4.07 3H,s),4.37(1H,m),5.30-5.54(2H,m),7.34 (1H,m),7.47(1H,s),7.47-7.60(2H,m),7. 93(1H,d,J=7.8Hz),8.43(1H,s),8.49(1H,d,J=9.0Hz).
IR($CHCl_3$):3397,3074,3027,3020,3009,2924,1738,1708,1647,1533,1534,1465, 1453 /cm.
$[\alpha]_D$=+43.7° (MeOH,c=1.01,25°C).

No.2a-188

[0297] $CDCl_3$ 300MHz
0.97(1H,d,J=10.2Hz),1.11 and 1.23(each 3H,each s),1.53-2.50(14H.m),4.2 3(1H,m),5.37-5.50(2H,m),8.10(1H,d, J=9.0Hz).6.20(1H,m),6.51(1H,m),6.97(1 H,m),10.81(1H,brs).
IR($CHCl_3$):3450,3236,3112,3029,3015,2925,2871,2645,1701,1616,1558,1516 /cm.
$[\alpha]_D$=+50.6° (MeOH,c=1.01,24°C).

No.2a-189

[0298] $CDCl_3$ 300MHz
0.94(1H,d,J=9.9Hz),1.11 and 1.23(each 3H,each s),1.50-2.46(14H,m),3.93(3H,s),4.18(1H,m),5.35-5.52(2H,m),6.03 (1H,d,J=9.3Hz),6.09(1H,m),-6.48(1H, m),6.73(1H,m).
IR($CHCl_3$):3452, 3102, 3028, 3007, 2925, 2871, 2666,1739,1 708,1650,1536,1499, 1471 /cm.
$[\alpha]_D$=+49.8° (MeOH,c=1.01,23°C).
m.p.101.5-103.5°C

No.2a-190

[0299] $CDCl_3$ 300MHz
0.94(1H,d,J=10.2Hz),1.11 and 1.21(each 3H,each s),1.54-2.47(14H,m),4.2 3(1H,m),5.33-5.52(2H,m),6.06(1H,d, J=9.OHz),6.34(1H,m),6.75(1H,m),6.36(1 H,m),9.71(1H,brs).
IR($CHCl_3$):3470,3215,3030,3020,3010,2925,2871,2664,1709,1613,1564,1510/cm.
$[\alpha]_D$=+43.3° (MeOH,c=1.01,24°C).

No.2a-191

[0300] $CDCl_3$ 300MHz
0.96(1H,d,J=10.2Hz),1.11 and 1.22(each 3H,each s),1.55-2.44(14H,m),3.6 6(3H,s),4.20(1H,m),5.35-5.51(2H,m),5.93 (1H,d,J=8.4Hz),6.27(1H,dd,J=1.8 and 2.7Hz),6.56(1H,t,J=2.7Hz),7.19(1H,t,J=1.8Hz).
IR($CHCl_3$):3452,3031,3018,3006,2925,2871,2662,1736,1710,1634,1609,1556, 1498 /cm.
$[\alpha]_D$=+43.1° (MeOH,c=1.01,23°C).

No.2a-192

[0301] $CDCl_3$ 300MHz
0.96(1H,d,J=10.5Hz),1.11 and 1.21(each 3H,each s),1.43(3H,t,J=7.5Hz),1. 54-2.44(14H,m),3.93(2H,q.J=7.5Hz).4.21 (1H.m),5.33.5.51(2H,m),5.94(1H,d, J=8.4Hz),6.27(1H,dd,J=1.8 and 2.7Hz),6.62(1H,t,J=2.7Hz),7.26(1H,t,J=1.8 Hz).
IR($CHCl_3$):3630,3452,3032,3018,3006,2925,2871,2661,1735,1710,1633,1610, 1555,1497 /cm.
$[\alpha]_D$=+40.1° (MeOH,c=1.00,23°C).

No.2a-193

[0302] $CDCl_3$ 300MHz
0.95(1H,d,J=10.2Hz), 1.10 and 1.22(each 3H,each s), 1.53-2.49(14H,m), 2.5 8(3H,s), 4.21(1H,m), 5.35-5.54(2H,m), 6.15(1H,d,J=8.1Hz), 6.52(1H,dd,J=1.8 and 3.6Hz), 7.29(1H,t,J=3.6Hz), 7.94(1H,t,J=1.8Hz).
IR($CHCl_3$):3516,3450,3410,3152,3027,3015,2925,2871,2670,1732,1648,1574, 1509 /cm.
$[\alpha]_D$=+45.0° (MeOH,c=1.01,25°C).

No.2a-194

[0303] $CDCl_3$ 300MHz
0.99(1H,d,J=10.2Hz),1.11 and 1.24(each 3H,each s),1.52-2.53(14H,m),4.3 4(1H,m),5.33-5.57(2H,m),6.21(1H,d, J=8.6Hz),7.35-7.50(2H,m),7.83(1H,s),7. 86(1H.m),.8.31 (1H,m).
IR($CHCl_3$):3443,3067,3013,2925,2870,2665,1708,1651,1515,1493 /cm.
$[\alpha]_D$=+55.7° (MeOH,c=1.01,23°C).

No.2a-195

[0304] $CDCl_3$ 300MHz
1.01(1H,d,J=10.0Hz),1.06 and 1.26(each 3H,each s),1.50-2.64(14H,m),2.6 8(3H,s),4.40(1H,m),5.36-5.61(2H,m),6.02 (1H,d,J=9.4Hz),7.30-7.42(2H,m),7. 73-7.86(2H,m).
IR($CHCl_3$):3510,3434.3062,3029,3014,2924,2871,2669,1708,1650,1563.1539, 1500 /cm.
$[\alpha]_D$=+72.4° (MeOH,c=1.00,23°C).
m.p.111.0-112.0°C

No.2a-196

[0305] $CDCl_3$ 300MHz
0.42 and 1.04(each 3H,each s),0.80(1H,d,J=10.0Hz),1.11-2.48(14H,m),2.2 4(3H,s),4.02(1H,m),5.23-5.44(2H,m),5.53 (1H,d,J=8.8Hz),7.27-7.31(2H,m),7. 42-7.48(3H,m),7.93(1H,s).
IR($CHCl_3$):3419,3114,3025,3006,2924,2871,2662,1737,1709,1636,1540,1519 /cm.
$[\alpha]_D$=+43.7° (MeOH,c=1.01,23°C).

No.2a-197

[0306] $CDCl_3$ 300MHz
0.95(1H,d,J=10.0Hz), 1.09 and 1.23(each 3H,each s), 1.54-2.46(18H,m), 2.7 7(4H,brs), 4.21(1H,m), 5.32-5.54(2H,m), 6.02(1H,d,J=8.6Hz), 7.43(1H,s).
IR($CHCl_3$):3445,3101,3024,3014,2928,2865,2661,1739,1708 1646,1550,1507 /cm.
$[\alpha]_D$=+51.9° (MeOH,c=1.01,23°C).

No.2a-198

[0307] $CDCl_3$ 300MHz
0.96(1H,d,J=10.2Hz),1.11 and 1.22(each 3H,each s),1.50-2.44(14H,m),4.2 4(1H,m),4.42(2H,s),5.35-5.49(2H,m),6.25 (1H,d,J=8.1Hz),7.33(1H,m),7.43(1 H,dd,J=1.5and 7.5Hz),7.49(1H,d,J=8.1Hz),7.60-7.63(1H,m),7.68(1H,dd,J=1. 8 and 7.8Hz),8.02(1H,d,J=1.8Hz),8.19(1H,dd,J=1.5 and 8.1Hz).
IR($CHCl_3$):3448,3030,3012,2925,2870,1739,1708,1671,1588,1559,1514,1472 /cm.
$[\alpha]_D$=+56.9° (MeOH,c=1.01,24°C).

No.2a-199

[0308] $CDCl_3$ 300MHz
0.96(1H,d,J=10.2Hz),1.11 and 1.22(each 3H,each s),1.51-2.46(14H,m),3.4 0(1H,m),3.76(1H,m),4.24(1H,m),5.33-5.51 (3H,m),6.25(1H,m),7.16(1H,m),7.2 4-7.33(2H,m),7.46(1H,d,J=7.5Hz),7.52-7.60(2H,m),7.85(1H,dd,J=1.8 and 4. 5Hz):
IR($CHCl_3$):3583,3447,3062,3028,3013,2924,2871,2663,1708,1651,1600,1557, 1514,1471 /cm.
$[\alpha]_D$=+54.8° (MeOH,c=1.00,23°C).

No.2a-200

[0309] $CDCl_3$ 300MHz
0.96(1H,d,J=10.2Hz),1.12 and 1.23(each 3H,each s),1.51-2.46(14H,m),4.2 5(1H,m),5.34-5.51(2H,m),6.25(1H,d, J=8.4Hz),7.02 and 7.10(each,1H,each d,J=12.3Hz),7.23-7.33(4H,m),7.50(1H,m),7.64(1H,dd,J=1.8 and 7.8Hz),7.8 2 (1H,d,J=1.8Hz).
IR($CHCl_3$):3450,3060,3025,3014,2925,2871,2662,1708,1653,1596,1542,1513, 1473 /cm.
$[\alpha]_D$=+62.5° (MeOH,c=1.00,24°C).

No.2a-201

[0310] $CDCl_3$ 300MHz
0.95(1H,d,J=9.9Hz),1.15 and 1.22(each 3H,each s),1.55-2.60(14H,m),4.26(1H,m),5.35-5.63(2H,m),7.14 (1H.d.J=9.9Hz),7.34 and 7.40(each,1H,each d, J=12.9Hz),7.62-7.73(4H,m),8.25-8.30(2H,m),8.72(1H,d,J=1.5Hz).
IR($CHCl_3$):3443,3389,3297,3061,3030,3016,2925 2870,1726,1708 1652,160 3;1521,1483,1472,1309 /cm.
$[\alpha]_D$=+61.1° (MeOH,c=1.01,23°C).

No.2a-202

[0311] $CDCl_3$ 300MHz
0.96(1H,d,J=10.2Hz),1.09 and 1.22(each 3H,each s),1.52-2.43(14H,m),2.6 3(3H,s),4.25(1H,m),5.33-5.49(2H,m),6.19 (1H,d,J=8.4Hz),7.10 and 7.58 (each, 2H,each d,J=9.0Hz),7.21(1H,m),7.30-7.32(2H,m),7.46(1H,d,J=7.5Hz)
IR($CHCl_3$):3511,3453,3062,3032,3014,2925 2870,1739,1708,1650,1595,1556, 1516,1482,1471 /cm.
$[\alpha]_D$=+60.2° (MeOH, c=1.01,25°C).

No.2a-203

[0312] $CDCl_3$ 300MHz
0.96(1H,d,J=10.5Hz),1.09 and 1.23(each 3H,each s), 1.52-2.43(14H,m),4.2 3(1H,m),5.35-5.51(2H,m),5.93(1H,d, J=8.7Hz),6.56(1H,dd,J=0.9 and 1.8Hz), 7.43(1H,t,J=1.8Hz),7.92(1H,dd,J=0.9 and 1.8Hz).
IR($CHCl_3$):3517,3450,3134,3031,3008,2925,2870,2667,1708,1656,1588,1570, 1514 /cm.
$[\alpha]_D$=+46.7° (MeOH,c=0.92,25°C).

No.2b-1

[0313] $[\alpha]_D$= +25.6° (MeOH,c=1.01,23°C).

No.2b-2

[0314] $[\alpha]_D$= +38.9° (MeOH,c=1.01,24°C).

No2c-1

[0315] $[\alpha]_D$= +60.5° (MeOH,c=1.01,22°C).

No.2c-2

[0316] $[\alpha]_D$= +55,8° (MeOH,c=0.92,22°C).

No.2c-3

[0317] $[\alpha]_D$= +54,7° (MeOH,c=1.01,22°C).

No.2d-1

[0318] $[\alpha]_D$= -6.2° (MeOH,c=1.00,21°C).

No.2d-2

[0319] $[\alpha]_D$=+15.8° (MeOH,c=0.34,22°C).

No.2d-3

[0320] $[\alpha]_D$=+31.6° (MeOH,c=1.01,22°C).

No.2e-1

[0321] $[\alpha]_D$= -9.4° (MeOH,c=1.00,22°C).

No.2e.2

[0322] $[\alpha]_D$= -1.8° (MeOH,c=1.02,23°C).

No.2e-3

[0323] $[\alpha]_D$= -6.7° (MeOH,c=1.01,23°C).

No.2f-1

[0324] $[\alpha]_D$= +6.8° (MeOH,c=1.01,23°C).

No.2f-2

[0325] $[\alpha]_D$= -2.6° (MeOH,c=1.00,22°C).

No.2f-3

[0326] $[\alpha]_D$= -3.5° (MeOH,c=1.01,22°C).

No.2g-1

[0327] $[\alpha]_D$= +54,6° (MeOH,c=1.01,24°C).

[0328] Compounds prepared in Examples above were tested for in vivo and in vitro activity according to the method shown in Experimental examples below.

Experiment 1 Binding to PGD_2 Receptor

Material and Method

(1) Preparation of Human Platelet Membrane Fraction

[0329] A Blood sample was obtained using a plastic syringe containing 3.8 % sodium citrate from veins of healthy volunteers (adult male and female), put into a plastic test tube and mixed gently by inversion. The sample was then centrifuged at 1800 rpm, 10 min at room temperature, and supernatant containing PRP (platelet rich plasma) was collected. The PRP was re-centrifuged at 2300 rpm, 22 min at room temperature to obtain platelets. The platelets were homogenized using a homogenizer (Ultra-Turrax) followed by centrifugation 3 times at 20,000 rpm, 10 min at 4°C to obtain a platelet membrane fraction. After protein determination, the membrane fraction was adjusted to 2 mg/ml and preserved in a refrigerator at -80°C until use.

(2) Binding to PGD_2 Receptor

[0330] To a binding-reaction solution (50 mM Tris/HCl, pH 7.4, 5 mM $MgCl_2$) (0.2 ml) were added human platelet membrane fraction (0.1 mg) and 5 nM [^{3}H]PGD_2 (115Ci/mmal), and reacted at 4°C for 90 min. After the reaction finished, the reaction mixture was filtered through a glass fiber filter paper, washed several times with cooled saline, and measurement made of radioactivity retained on the filter paper. The specific binding was calculated by subtracting the non-

specific binding (the binding in the presence of 10 μM PGD_2) from the total binding. The binding-inhibitory activity of each compound was expressed as concentration required for 50 % inhibition (IC_{50}), which was determined by depicting a substitution curve by plotting the binding ratio (%) in the presence of each compound, where the binding ratio in the absence of a test compound is - 100 %. The results are shown in Table below.

Compound number	Activity (μM)	compound number	activity (μM)
2a-4	0.54		
2a-17	0.12		
2a-21	5.2		
2a-28	0.046		
2a-95	1.6		
2a-109	0.003		

Experiment 2 Evaluation of Antagonistic Activity Against PGD_2 Receptor Using Human Platelet

[0331] Peripheral blood was obtained from a healthy volunteer using a syringe in which 1/9 volume of citric acid/dextrose solution had been previously added. The syringe was subjected to centrifugation at 180 g for 10 min to obtain the supernatant (PRP: platelet rich plasma). The resultant RRP was washed 3 times with a washing buffer and the number of platelets was counted with a micro cell counter. A suspension adjusted to contain platelets at a final concentration of 5 x 10^8/ml was warmed at 37°C, and then subjected to the pretreatment with 3-isobutyl-1-methylxanthine (0.5mM) for 5 min. To the suspension was added a test compound diluted at various concentrations. Ten-minutes later, the reaction was induced by the addition of 0.1-2.0 μM PGD_2 and, 15-minutes later, stopped by the addition of HC1. The platelets were destroyed with an ultrasonic homogenizer. After centrifugation, the cAMP in the supernatant was determined by radioassay. PGD_2 receptor antagonism of a drug was evaluated as follows. The inhibition rate regarding cAMP increased by the addition of PGD_2 was determined at individual concentration, and then the concentration of the drug required for 50 % inhibition (IC_{50}) was calculated. The results are shown in the Table below.

Compound number	Inhibition of Increase of Human Platelet cAMP (IC_{50})(μM)
2a-2	0.77
2a-4	0.49
2a-35	1.52
2a-75	0.71

Experiment 3 Experiment Using Nasal Occlusion Model

[0332] The method used for measuring the nasal cavity resistance and evaluating the anti-nasal occlusion using a guinea pig are described below.

[0333] A 1% ovalbumin (OVA) solution was treated with an ultrasonic nebulizer to obtain an aerosol. A Hartley male guinea pig was sensitized by inhaling twice the aerosol for 10 min at one-week intervals. Seven-days after the sensitization, the guinea pig was exposed to an antigen to initiate the reaction. Then the trachea was incised under anesthesia with pentobarbital (30 mg/kg, i.p.) and cannulas were inserted into -the trachea at the pulmonary and nasal cavity sides. The canal inserted at the pulmonary side was connected with-an artificial respirator that provides 4 ml air 60 times/min. After arresting the spontaneous respiration of a guinea pig with Garamin (2 mg/kg, i.v.), air was supplied to the snout side with an artificial respirator at the frequency of 70 times/min, and the flow rate of 4 ml air/time, and the atmospheric pressure required for the aeration was measured by the use of a transducer fitted at the branch. The measurement was used as a parameter of the nasal cavity resistance. The exposure of an antigen was carried out by generating aerosol of 3 % OVA solution for 3 min between the respirator and nasal cavity cannula. The test drug was injected intravenously 10 min before the antigen exposure. The nasal resistance between 0 to 30 min was measured continuously and the effect was expressed as inhibition rate to that obtained for vehicle using the AUC for 30 min (on the vertical axis, nasal cavity resistance (cm H_2O), and on the horizontal axis, time (0 - 30 min)) as an indication. The result is shown below.

Compound number	Inhibition Rate (%) 1 mg/kg (i.v.)	Remarks
2a-4	60	
2a-21	52	

(continued)

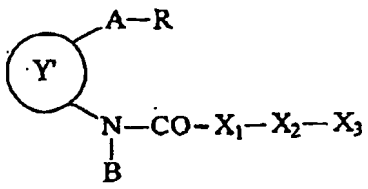
Compound number	Inhibition Rate (%) 1 mg/kg (i.v.)	Remarks
2a-28	54	
2a-95	77	
2a-96	77	10mg/kg(p.o.)
2a-109	73	
2a-110	66	10mg/kg(p.o.)
22a-194	79	

Formulation 1 Preparation of Tablets

[0334] Tablets each containing 40 mg of active ingredient were prepared in a conventional manner.

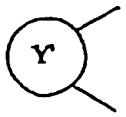
Claims

1. A compound of the formula (Ib) :

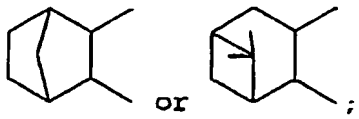


(Ib)

wherein



is



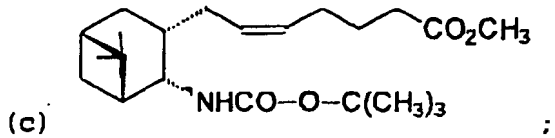
;

wherein A is alkylene which optionally is intervened by hetero atom or phenylene, contains oxo group, and/or has an unsaturated bond;

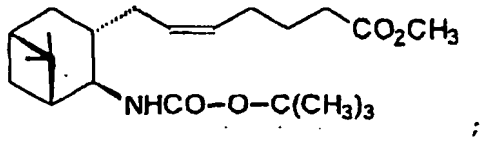
B is hydrogen, alkyl, aralkyl or acyl;
R is $COOR_1$, CH_2OR_2 or $CON(R_3)R_4$;
R_1 is hydrogen or alkyl;
R_2 is hydrogen or alkyl;
R_3 and R_4 each are independently hydrogen, alkyl, hydroxy or alkylsulfonyl;
X_1 is a single bond, phenylene, naphthylene, thiophenediyl, indolediyl, or oxazolediyl;
X_2 is a single bond, -N=N-, -N=CH-, -CH=N-, -CH=N-N-, -CH=N-O-, -C=NNHCSNH-, -C=NNHCONH-, -CH=CH-, -CH(OH)-, -C(Cl)=C(Cl)-, $-(CH_2)_n-$, ethynylene, $-N(R_5)-$, $-N(R_{51})CO-$, $-N(R_{52})SO_2-$, $-N(R_{53})CON(R_{54})-$, $-CON(R_{55})-$ $-SO_2N(R_{56})-$, -O-, -S-, -SO-, $-SO_2-$, -CO-, oxadiazolediyl, thiadiazolediyl or tetrazolediyl;
X_3 is alkyl, alkenyl, alkynyl, aryl, aralkyl, heterocyclic group, cycloalkyl, cycloalkenyl, thiazolinylidenemethyl,

thiazolidinylidenemethyl, -CH=NR$_6$ or -N=C(R$_7$)R$_8$;
R$_5$, R$_{51}$, R$_{52}$, R$_{53}$, R$_{54}$, R$_{55}$ and R$_{56}$, each are hydrogen or alkyl;
R$_6$ is hydrogen, alkyl, hydroxy, alkoxy, carbamoyloxy, thiocarbamoyloxy, ureido or thioureido;
R$_7$ and R$_8$ each are independently alkyl, alkoxy or aryl;
and n is 1 or 2;

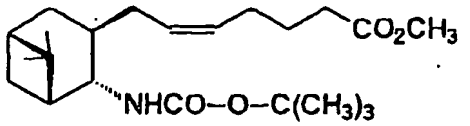
wherein a cyclic substituent may have one to three substituents selected from the group consisting of nitro, alkoxy, sulfamoyl, substituted- or unsubstituted-amino, acyl, acyloxy, hydroxy, halogen, alkyl, alkynyl, carboxy, alkoxycarbonyl, aralkoxycarbonyl, aryloxycarbonyl, mesyloxy, cyano, alkenyloxy, hydroxyalkyl, trifluoromethyl, alkylthio, -N=PPh$_3$, oxo, thioxo, hydroxyimino, alkoxyimino, phenyl and alkylenedioxy, or its salt or hydrate thereof; with the proviso that compounds (a) wherein X$_1$ and X$_2$ are a single bond, and X$_3$ is phenyl; (b) wherein X$_1$ is a single bond, X$_2$ is -O-, and X$_3$ is benzyl;



(c) ;

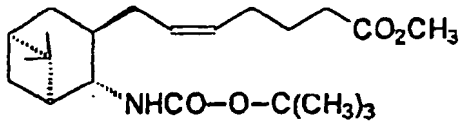


(d) ;



(e) ;

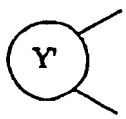
and



(f)

are excluded.

2. The compound of claim 1, a salt or hydrate thereof, wherein



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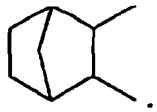
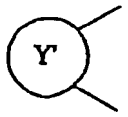


3. The compound of claim 2, a salt or hydrate thereof, wherein R is $COOR_1$.

4. The compound of claim 2, salt or hydrate thereof,
wherein X_1 is phenylene or thiophenediyl, X_2 is a single bond, -N=N-, -CH=CH-, ethynylene, -O-, -S-, -CO-, -CON(R_{55})-, -N(R_{51})CO- and X_3 is phenyl or thienyl.

5. The compound of claim 1, a salt or hydrate thereof, wherein



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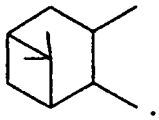
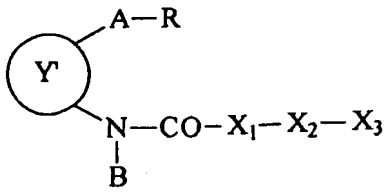


6. The compound of claim 5, a salt or hydrate thereof, wherein B is hydrogen, both X_1 and X_2 are a single bond, X_3 is thienyl, thiazolyl, thiadiazolyl, isothiazolyl, pyrrolyl, pyridyl, benzofuryl, benzimidazolyl, benzothienyl, dibenzofuryl, dibenzothienyl, quinolyl or indolyl.

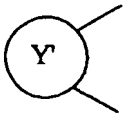
7. The compound of claim 5, a salt or hydrate thereof, wherein X_1 is phenylene, thiophenediyl, indolediyl or oxazolediyl, X_2 is a single bond, -N=N-, -CH=CH-, ethynylene, -S- or -O-, and X_3 is aryl or heterocyclic group.

8. A compound of the formula (Ib) below, for use in a method of treating diseases in which mast cell dysfunction is involved, tracheal contraction, asthma, allergic rhinitis, allergic conjunctivitis, urticaria, injury due to ischemic reperfusion, nasal occlusion and inflammation:

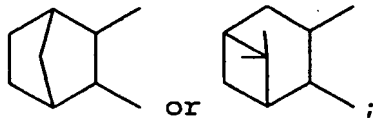


(Ib)

wherein



is



wherein A is alkylene which optionally is intervened by hetero atom or phenylene, contains oxo group, and/or has an unsaturated bond;

B is hydrogen, alkyl, aralkyl or acyl;
R is $COOR_1$, CH_2OR_2 or $CON(R_3)R_4$;
R_1 is hydrogen or alkyl;
R_2 is hydrogen or alkyl;
R_3 and R_4 each are independently hydrogen, alkyl, hydroxy or alkylsulfonyl;
X_1 is a single bond, phenylene, naphthylene, thiophenediyl, indolediyl, or oxazolediyl;
X_2 is a single bond, -N=N-, -N=CH-, -CH=N-, -CH=N-N-, -CH=N-O-, -C=NNHCSNH-, -C=NNHCONH-, -CH=CH-, -CH(OH)-, -C(Cl)=C(Cl)-, $-(CH_2)_n-$, ethynylene, $-N(R_5)-$, $-N(R_{51})CO-$, $-N(R_{52})SO_2-$, $-N(R_{53})CON(R_{54})-$, $-CON(R_{55})-$ $-SO_2N(R_{56})-$, -O-, -S-, -SO-, $-SO_2-$ -CO-, oxadiazolediyl, thiadiazolediyl or tetrazolediyl;
X_3 is alkyl, alkenyl, alkynyl, aryl, aralkyl, heterocyclic group, cycloalkyl, cycloalkenyl, thiazolinylidenemethyl, thiazolidinylidenemethyl, $-CH=NR_6$ or $-N=C(R_7)R_8$;
R_5, R_{51}, R_{52}, R_{53}, R_{54}, R_{55} and R_{56}, each are hydrogen or alkyl;
R_6 is hydrogen, alkyl, hydroxy, alkoxy, carbamoyloxy, thiocarbamoyloxy, ureido or thioureido;
R_7 and R_8 each are independently alkyl, alkoxy or aryl; and n is 1 or 2;

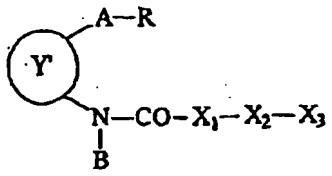
wherein a cyclic substituent may have one to three substituents selected from the group consisting of nitro, alkoxy, sulfamoyl, substituted- or unsubstituted-amino, acyl, acyloxy, hydroxy, halogen, alkyl, alkynyl, carboxy, alkoxycarbonyl, aralkoxycarbonyl, aryloxycarbonyl, mesyloxy, cyano, alkenyloxy, hydroxyalkyl, trifluoromethyl, alkylthio, $-N=PPh_3$, oxo, thioxo, hydroxyimino, alkoxyimino, phenyl and alkylenedioxy, or its salt or hydrate thereof; with the proviso that compounds (a) wherein X_1 and X_2 are a single bond, and X_3 is phenyl; and (b) wherein X_1 is a single bond, X_2 is -O-, and X_3 is benzyl are excluded.

9. Use of a PGD_2 antagonist comprising a compound of the formula (Ib) as defined in claim 8, or a salt or a hydrate thereof, as an active ingredient in the manufacture of a pharmaceutical composition for the treatment of diseases in which mast cell dysfunction is involved, tracheal contraction, asthma, allergic rhinitis, allergic conjunctivitis, urticaria, injury due to ischemic reperfusion, nasal occlusion and inflammation.

10. Use of a PGD_2 antagonist comprising a compound of the formula (Ib) as defined in claim 9, or a salt or a hydrate thereof, as an active ingredient in the manufacture of a pharmaceutical composition for the treatment of diseases in which mast cell dysfunction is involved, tracheal contraction, asthma, allergic rhinitis, allergic conjunctivitis, urticaria, injury due to ischemic reperfusion, nasal occlusion and inflammation.

Patentansprüche

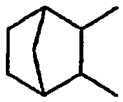
1. Verbindung der Formel (Ib):



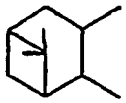
(Ib)

wobei

für



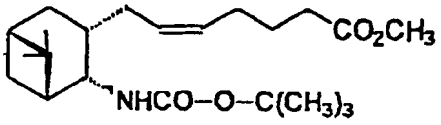
oder



steht,
wobei A Alkylen ist, das gegebenenfalls durch ein Heteroatom oder Phenylen unterbrochen sein kann, eine Oxogruppe enthält und/oder eine ungesättigte Bindung aufweist;

B Wasserstoff, Alkyl, Aralkyl oder Acyl ist;
R für $COOR_1$, CH_2OR_2 oder $CON(R_3)R_4$ steht;
R_1 Wasserstoff oder Alkyl ist;
R_2 Wasserstoff oder Alkyl ist;
R_3 und R_4 jeweils unabhängig Wasserstoff, Alkyl, Hydroxy oder Alkylsulfonyl sind;
X_1 eine Einfachbindung, Phenylen, Naphthylen, Thiophendiyl, Indoldiyl oder Oxazoldiyl ist;
X_2 eine Einfachbindung, -N=N-, -N=CH-, -CH=N-, -CH=N-N-, -CH=N-O-, -C=NNHCSNH-, -C=NNHCONH-, -CH=CH-, -CH(OH)-, -C(Cl)=C(Cl)-, $-(CH_2)_n-$, Ethinylen, $-N(R_5)-$, $-N(R_{51})CO-$, $-N(R_{52})SO_2-$, $-N(R_{53})CON(R_{54})-$, $-CON(R_{55})--SO_2N(R_{56})-$, -O-, -S-, -SO-, $-SO_2-$, -CO-, Oxadiazoldiyl, Thiadiazoldiyl oder Tetrazoldiyl ist;
X_3 Alkyl, Alkenyl, Alkinyl, Aryl, Aralkyl, ein heterocyclischer Rest, Cycloalkyl, Cycloalkenyl, Thiazolinylidenmethyl, Thiazolidinylidenmethyl, $-CH=NR_6$ oder $-N=C(R_7)R_8$ ist;
R_5, R_{51}, R_{52}, R_{53}, R_{54}, R_{55} und R_{56} jeweils Wasserstoff oder Alkyl sind;
R_6 Wasserstoff, Alkyl, Hydroxy, Alkoxy, Carbamoyloxy, Thiocarbamoyloxy, Ureido oder Thioureido ist;
R_7 und R_8 jeweils unabhängig Alkyl, Alkoxy oder Aryl sind;
und n gleich 1 oder 2 ist;

wobei ein cyclischer Substituent 1 bis 3 Substituenten, ausgewählt aus Nitro, Alkoxy, Sulfamoyl, substituiertem oder unsubstituiertem Amino, Acyl, Acyloxy, Hydroxy, Halogen, Alkyl, Alkinyl, Carboxy, Alkoxycarbonyl, Aralkoxycarbonyl, Aryloxycarbonyl, Mesyloxy, Cyano, Alkenyloxy, Hydroxyalkyl, Trifluormethyl, Alkylthio, $-N=PPh_3$, Oxo, Thioxo, Hydroxyimino, Alkoxyimino, Phenyl und Alkylendioxy oder deren Salzen oder Hydraten davon, aufweisen kann; mit der Maßgabe, dass die Verbindungen (a), wobei X_1 und X_2 Einfachbindungen sind und X_3 Phenyl ist; (b), wobei X_1 eine Einfachbindung ist, X_2 für -O- steht und X_3 Benzyl ist;

(c) 

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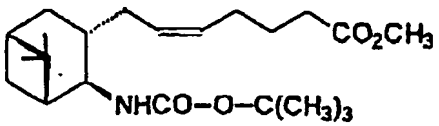
(d) 

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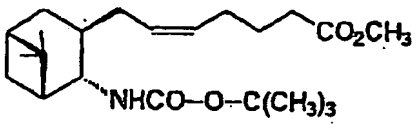
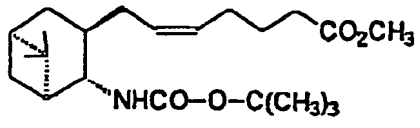
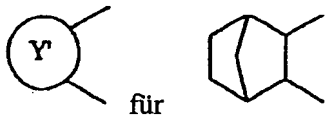
(e) 

und

(f) 

ausgenommen sind.

2. Verbindung nach Anspruch 1, ein Salz oder Hydrat davon, wobei

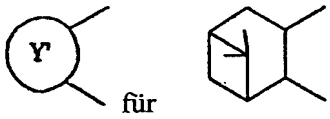


steht.

3. Verbindung nach Anspruch 2, ein Salz oder Hydrat davon, wobei R für $COOR_1$ steht.

4. Verbindung nach Anspruch 2, ein Salz oder Hydrat davon, wobei X_1 Phenylen oder Thiophendiyl ist, X_2 eine Einfachbindung, -N=N-, -CH=CH-, Ethinylen, -O-, -S-, -CO-, $-CON(R_{55})-$, $-N(R_{51})CO-$ ist und X_3 Phenyl oder Thienyl ist.

5. Verbindung nach Anspruch 1, ein Salz oder Hydrat davon, wobei

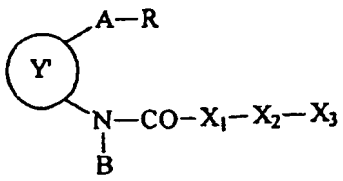


steht.

6. Verbindung nach Anspruch 5, ein Salz oder Hydrat davon, wobei B Wasserstoff ist, X_1 und X_2 beide eine Einfachbindung sind, X_3 Thienyl, Thiazolyl, Thiadiazolyl, Isothiazolyl, Pyrrolyl, Pyridyl, Benzofuryl, Benzimidazolyl, Benzothienyl, Dibenzofuryl, Dibenzothienyl, Chinolyl oder Indolyl ist.

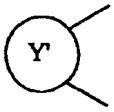
7. Verbindung nach Anspruch 5, ein Salz oder Hydrat davon, wobei X_1 Phenylen, Thiophendiyl, Indoldiyl oder Oxazoldiyl ist, X_2 eine Einfachbindung, -N=N-, -CH=CH-, Ethinylen, -S- oder -O- ist und X_3 Aryl oder ein heterocyclischer Rest ist.

8. Verbindung der nachstehenden Formel (Ib), zur Verwendung in einem Verfahren zur Behandlung von Krankheiten, die eine Fehlfunktion der Mastzellen einschließen, trachealer Kontraktion, Asthma, allergischer Rhinitis, allergischer Konjunktivitis, Urtikaria, Verletzungen aufgrund von Ischämie-Reperfusion, Nasenokklusion und Entzündung:

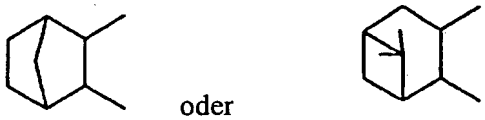


(Ib)

wobei



für



steht;
wobei A Alkylen ist, das gegebenenfalls durch ein Heteroatom oder Phenylen unterbrochen sein kann, eine Oxogruppe enthält und/oder eine ungesättigte Bindung aufweist;

B Wasserstoff, Alkyl, Aralkyl oder Acyl ist;
R für $COOR_1$, CH_2OR_2 oder $CON(R_3)R_4$ steht;
R_1 Wasserstoff oder Alkyl ist;
R_2 Wasserstoff oder Alkyl ist;
R_3 und R_4 jeweils unabhängig Wasserstoff, Alkyl, Hydroxy oder Alkylsulfonyl sind;
X_1 eine Einfachbindung, Phenylen, Naphthylen, Thiophendiyl, Indoldiyl oder Oxazoldiyl ist;
X_2 eine Einfachbindung, -N=N-, -N=CH-, -CH=N-, -CH=N-N-, -CH=N-O-, -C=NNHCSNH-, -C=NNHCONH-, -CH=CH-, -CH(OH)-, -C(Cl)=C(Cl)-, $-(CH_2)_n-$, Ethinylen, $-N(R_5)-$, $-N(R_{51})CO-$, $-N(R_{52})SO_2-$, $-N(R_{53})CON(R_{54})-$, $-CON(R_{55})-$, $-SO_2N(R_{56})-$, -O-, -S-, -SO-, $-SO_2-$, -CO-, Oxadiazoldiyl, Thiadiazoldiyl oder Tetrazoldiyl ist;
X_3 Alkyl, Alkenyl, Alkinyl, Aryl, Aralkyl, ein heterocyclischer Rest, Cycloalkyl, Cycloalkenyl, Thiazolinylidenmethyl, Thiazolidinylidenmethyl, $-CH=NR_6$ oder $-N=C(R_7)R_8$ ist;
R_5, R_{51}, R_{52}, R_{53}, R_{54}, R_{55} und R_{56} jeweils Wasserstoff oder Alkyl sind;
R_6 Wasserstoff, Alkyl, Hydroxy, Alkoxy, Carbamoyloxy, Thiocarbamoyloxy, Ureido oder Thioureido ist;
R_7 und R_8 jeweils unabhängig Alkyl, Alkoxy oder Aryl sind;
und n gleich 1 oder 2 ist;

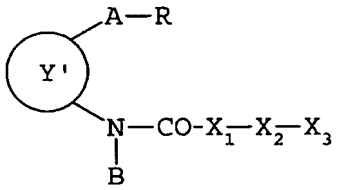
wobei ein cyclischer Substituent 1 bis 3 Substituenten, ausgewählt aus Nitro, Alkoxy, Sulfamoyl, substituiertem oder unsubstituiertem Amino, Acyl, Acyloxy, Hydroxy, Halogen, Alkyl, Alkinyl, Carboxy, Alkoxycarbonyl, Aralkoxycarbonyl, Aryloxycarbonyl, Mesyloxy, Cyano, Alkenyloxy, Hydroxyalkyl, Trifluormethyl, Alkylthio, $-N=PPh_3$, Oxo, Thioxo, Hydroxyimino, Alkoxyimino, Phenyl und Alkylendioxy oder deren Salzen oder Hydraten davon, aufweisen kann; mit der Maßgabe, dass die Verbindungen (a), wobei X_1 und X_2 Einfachbindungen sind und X_3 Phenyl ist; und (b), wobei X_1 eine Einfachbindung ist, X_2 für -O- steht und X_3 Benzyl ist, ausgenommen sind.

9. Verwendung eines PGD_2-Antagonisten, umfassend eine Verbindung der Formel (Ib) wie in Anspruch 8 definiert oder ein Salz oder Hydrat davon als wirksamen Bestandteil bei der Herstellung eines Arzneimittels zur Behandlung von Krankheiten, die eine Fehlfunktion der Mastzellen einschließen, trachealer Kontraktion, Asthma, allergischer Rhinitis, allergischer Konjunktivitis, Urtikaria, Verletzungen aufgrund von Ischämie-Reperfusion, Nasenokklusion und Entzündung.

10. Verwendung eines PGD_2-Antagonisten, umfassend eine Verbindung der Formel (Ib) wie in Anspruch 9 definiert oder ein Salz oder Hydrat davon als wirksamen Bestandteil bei der Herstellung eines Arzneimittels zur Behandlung von Krankheiten, die eine Fehlfunktion der Mastzellen einschließen, trachealer Kontraktion, Asthma, allergischer Rhinitis, allergischer Konjunktivitis, Urtikaria, Verletzungen aufgrund von Ischämie-Reperfusion, Nasenokklusion und Entzündung.

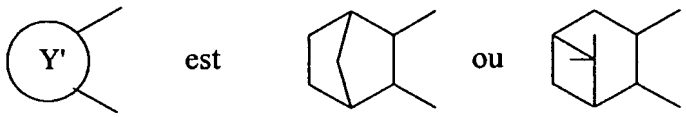
Revendications

1. Composé de formule (Ib) :



(Ib)

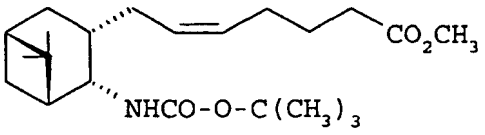
dans laquelle



A est alkylène qui, le cas échéant, est interrompu par (au moins) un hétéroatome ou phénylène, contient un groupe oxo, et/ou a (au moins) une liaison insaturée ;
B est hydrogène, alkyle, aralkyle ou acyle ;
R est $COOR_1$, CH_2OR_2 ou $CON(R_3)R_4$;
R_1 est hydrogène ou alkyle ;
R_2 est hydrogène ou alkyle ;
R_3 et R_4 représentent chacun indépendamment hydrogène, alkyle, hydroxy ou alkylsulfonyle ;
X_1 est une simple liaison, phénylène, naphtylène, thiophènediyle, indolediyle, ou axazolediyle ;
X_2 est une simple liaison, -N=N-, -N=CH-, -CH=N-, -CH=N-N-, -CH=N-O-, -C=NNHCSNH-, -C=NNHCONH-, -CH=CH-, -CH(OH)-, -C(C1)=C(C1)-, $-(CH_2)_n-$, éthynylène, $-N(R_5)-$, $-N(R_{51})CO-$, $-N(R_{52})SO_2-$, $-N(R_{53})CON(R_{54})-$, $-CON(R_{55})-$, $-SO_2N(R_{56})-$, -O-, -S-, -SO-, $-SO_2-$, -CO-, oxadiazolediyle, thiadiazolediyle ou tétrazolediyle ;
X_3 est alkyle, alkényle, alkynyle, aryle, aralkyle, groupe hétérocyclique, cycloalkyle, cycloalkényle, thiazolinylidèneméthyle, thiazolidinylidèneméthyle, $-CH=NR_6$, ou $-N=C(R_7)R_8$;
R_5, R_{51}, R_{52}, R_{53}, R_{54}, R_{55} et R_{56} sont chacun hydrogène ou alkyle ;
R_6 est hydrogène, alkyle, hydroxy, alkoxy, carbamoyloxy, thiocarbamoyloxy, uréido ou thiouréido ;
R_7 et R_8 sont indépendamment chacun alkyle, alkoxy ou aryle ; et
n est 1 ou 2 ;
un substituant cyclique pouvant avoir de 1 à 3 substituants choisis parmi l'ensemble constitué par les nitro, alkoxy, sulfamoyle, amino substitué ou non substitué, acyle, acyloxy, hydroxy, halogéno, alkyle, alkynyle, carboxy, alkoxycarbonyle, aralkoxycarbonyle, aryloxycarbonyle, mésyloxy, cyano, alkényloxy, hydroxyalkyle, trifluorométhyle, alkylthio, $-N=PPh_3$, oxo, thioxo, hydroxyimino, alkoxyimino, phényle et alkylènedioxy ;

ou ses sels ou ses hydrates ;
avec la condition que les composés

(a) dans lesquels X_1 et X_2 sont une simple liaison, et X_3 est phényle ;
(b) dans lesquels X_1 est une simple liaison, X_2 est -O-, et X_3 est benzyle ;
(c)



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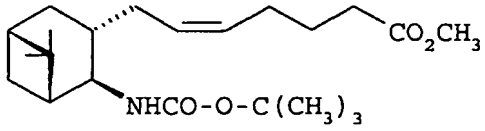
(d)



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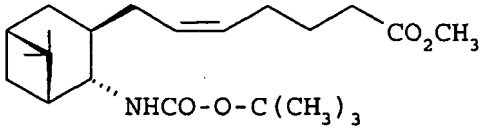
(e)



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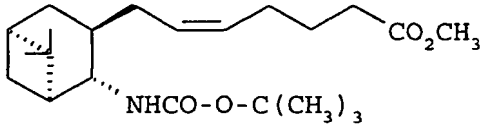
et
(f)



sont exclus.

2. Composé suivant la revendication 1, ses sels ou hydrates, où

.

3. Composé suivant la revendication 2, ses sels ou hydrates, où R est $COOR_1$.

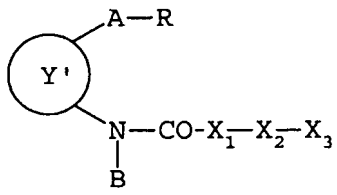
4. Composé suivant la revendication 2, ses sels ou hydrates, où X_1 est phénylène ou thiophènediyle, X_2 est une simple liaison, -N=N-, -CH=CH-, éthynylène, -O-, -S-, -CO-, $-CON(R_{55})-$, $-N(R_{51})CO-$, et X_3 est phényle ou thiényle.

5. Composé suivant la revendication 1, ses sels ou hydrates, où

6. Composé suivant la revendication 5, ses sels ou hydrates, où B est hydrogène, X_1 et, X_2 représentent chacun une simple liaison, et X_3 est thiényle, thiazolyle, thiadiazolyle, isothiazolyle, pyrrolyle, pyridyle, benzofuryle, benzimidazolyle, benzothiényle, dibenzofuryle, dibenzothiényle, quinolyle ou indolyle.

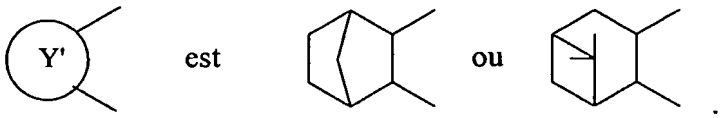
7. Composé suivant la revendication 5, ses sels ou hydrates, où X_1 est phénylène, thiophènediyle, indolediyle ou oxazolediyle, X_2 une simple liaison, -N=N-, -CH=CH-, éthynylène, -S- ou -O-, et X_3 est aryle ou un groupe hétérocyclique.

8. Composé de formule (Ib) ci-après, pour utilisation dans le traitement de maladies impliquant un disfonctionnement mastocytaire, la contraction trachéale, l'asthme, la rhinite allergique, la conjonctivite allergique, l'urticaire, le trouble dû à la reperfusion ischémique, l'occlusion nasale et l'inflammation :



(Ib)

dans laquelle



;

A est alkylène qui, le cas échéant, est interrompu par (au moins) un hétéroatome ou phénylène, contient un groupe oxo, et/ou a (au moins) une liaison insaturée ;
B est hydrogène, alkyle, aralkyle ou acyle ;
R est $COOR_1$, CH_2OR_2 ou $CON(R_3)R_4$;
R_1 est hydrogène ou alkyle ;
R_2 est hydrogène ou alkyle ;
R_3 et R_4 représentent indépendamment chacun hydrogène, alkyle, hydroxy ou alkylsulfonyle ;
X_1 est une simple liaison, phénylène, naphtylène, thiophènediyle, indolediyle, ou oxazolediyle ;
X_2 est une simple liaison, -N=N-, -N=CH-, -CH=N-, -CH=N-N-, -CH=N-O-, -C=NNHCSNH-, -C=NNHCONH-, -CH=CH-, -CH(OH)-, -C(C1)=C(C1)-, $-(CH_2)_n-$, éthynylène, $-N(R_5)-$, $-N(R_{51})CO-$, $-N(R_{52})SO_2-$, $-N(R_{53})CON(R_{54})-$, $-CON(R_{55})-$, $-SO_2N(R_{56})-$, -O-, -S-, -SO-, $-SO_2-$, -CO-, oxadiazolediyle, thiadiazolediyle ou tétrazolediyle ;
X_3 est alkyle, alkényle, alkynyle, aryle, aralkyle, groupe hétérocyclique, cycloalkyle, cycloalkényle, thiazolinylidèneméthyle, thiazolidinylidèneméthyle, $-CH=NR_6$, ou $-N=C(R_7)R_8$;
R_5, R_{51}, R_{52}, R_{53}, R_{54}, R_{55} et R_{56} sont chacun hydrogène ou alkyle ;
R_6 est hydrogène, alkyle, hydroxy, alkoxy, carbamoyloxy, thiocarbamoyloxy, uréido ou thiouréido ;
R_7 et R_8 représentent indépendamment chacun alkyle, alkoxy ou aryle ; et n est 1 ou 2 ;

un substituant cyclique pouvant avoir de 1 à 3 substituants choisis parmi l'ensemble constitué par les nitro, alkoxy, sulfamoyle, amino substitué ou non substitué, acyle, acyloxy, hydroxy, halogéno, alkyle, alkynyle, carboxy, alkoxycarbonyle, aralkoxycarbonyle, aryloxycarbonyle, mésyloxy, cyano, alkényloxy, hydroxyalkyle, trifluorométhyle, alk-

ylthio, -N=PPh$_3$, oxo, thioxo, hydroxyimino, alkoxylmino, phényle et alkylènedioxy ;
ou ses sels ou ses hydrates ;
avec la condition que les composés

(a) dans lesquels X_1 et X_2 sont une simple liaison, et X_3 est phényle ; et
(b) dans lesquels X_1 est une simple liaison, X_2 est -O-, et X_3 est benzyle sont exclus.

9. Utilisation d'un antagoniste de PGD_2 comprenant un composé de formule (Ib) tel que défini dans la revendication 8, l'un de ses sels ou hydrates, en tant qu'ingrédient actif dans la préparation d'une composition pharmaceutique pour le traitement de maladies impliquant un disfonctionnement mastocytaire, la contraction trachéale, l'asthme, la rhinite allergique, la conjonctivite allergique, l'urticaire, le trouble dû à la reperfusion ischémique, l'occlusion nasale et l'inflammation.

10. Utilisation d'un antagoniste de PGD_2 comprenant un composé de formule (Ib) tel que défini dans la revendication 9, l'un de ses sels ou hydrates, en tant qu'ingrédient actif dans la préparation d'une composition pharmaceutique pour le traitement de maladies impliquant un disfonctionnement mastocytaire, la contraction trachéale, l'asthme, la rhinite allergique, la conjonctivite allergique, l'urticaire, le trouble dû à la reperfusion ischémique, l'occlusion nasale et l'inflammation.